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ABSTRACTS

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ORAL PRESENTATIONS

Acute Kidney Injury (including CKRT)

O-01 - Electrolyte disturbances and their relationship with tubular dysfunction in paediatric critical care

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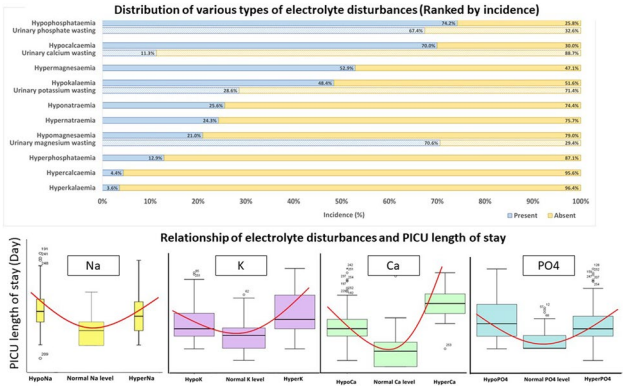
Introduction: Electrolyte disturbances are common yet overlooked conditions in paediatric critical care. We described the epidemiology of electrolyte disturbances and their impact on critically ill children.
Methods: We conducted a prospective cohort study recruiting children aged 1 month to 18 years old from 6/2020 to 6/2021 admitted to the paediatric intensive care unit (PICU) of the Hong Kong Children's Hospital. The serum electrolytes profiles on sodium, potassium, calcium, phosphate and magnesium levels were collected. Appropriate urinary investigations for tubular function were performed among children with electrolyte disturbances.
Findings: There were 254 episodes of admission identified for analysis. Male accounted for 58.3% and the median (interquartile range) age was 4.9 (9.6) years old. 94.9% of children had electrolyte disturbances, and the median number of types of electrolyte disturbances was 3 (2) types. Figure 1 showed the incidences of different types of disturbances. Several conditions including history of malignancy (p=0.007), bone marrow transplantation recipient (p=0.036), AKI (p<0.001), requirement of inotropes (p<0.001) and ventilatory support (p<0.001) were associated with higher degree of electrolyte disturbances. A high proportion of urinary wasting of magnesium (70.6%), phosphate (67.4%) and potassium (28.6%) were observed among those with hypomagnesaemia, hypophosphataemia and hypokalaemia. Among children with ≥2 types of electrolytes disturbances, the median degree of aminoaciduria was 19.1(52.4)% and 62.6% showed elevated urinary beta-2-microglobulin level (median: 2.2[6.9]μg/ml). Tubular dysfunction occurred independent of AKI. Electrolyte disturbances was associated with increased duration of ventilation (p<0.001), PICU length of stay (p<0.001) and mortality (p<0.001). A U-shaped relationship could be observed among various serum electrolyte levels and the PICU length of stay (Figure 1). 71.3% of children required electrolytes supplementation during PICU stay.
Conclusion: Electrolyte disturbances were commonly observed in PICU. The degree of disturbances was associated with both PICU morbidity and mortality. Proximal tubular dysfunction was associated with multiple electrolytes disturbances.



Acute Kidney Injury (including CKRT)

O-02 - Epidemiology and Outcome of Acute Kidney Injury in Children from Western India- retrospective multicentric study by the Kidney Foundation for Children

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Indian studies on AKI are single centre studies with their inherent bias. This multicentric retrospective observational study was undertaken

to study the regional epidemiology and outcome of AKI in children treated at facilities with varying resources.
Children aged one month to 18 years who were hospitalized with or developed AKI in hospital as defined by KDIGO criteria were included. Risk factors analyzed include current illness, pre-existing renal disease, mechanical ventilation, vasoactive drugs, contrast and nephrotoxic medication. Outcome was analyzed by patient survival and renal outcome as complete, partial or no recovery.
530 children (316boys, 214girls) from 18 centres had AKI, 326 [61.51%] from public and 204 [38.49%] from private hospitals. There were 123 [23.21%] infants; 270 [50.94%] were older than 12 years. At presentation, 184 [34.72%] were in stage1, 132 [24.91%] in stage2, and 214 [40.38%] in stage3. Underlying nephro-urological disorder was identified in 203 [38.30%]. Infection was the trigger in 240 [45.28%]. 301 [56.79%] patients satisfied both urine output and serum creatinine criteria for diagnosis, 15 [2.83%] met isolated urine output criteria. 238 [44.91%] patients received vasoactive drugs. 154 [29.06%] received nephrotoxic medications, Vancomycin was the commonest drug in 74 [13.96%]. 159 [30%] received dialysis; 67 [42.14%] received intermittent PD with stiff catheter, 39 [24.53%] intermittent HD, 24 [15.09%] continuous PD (soft catheter), 7 [4.40%] SLED and 3 [1.89%] CRRT. Complete renal recovery was seen among 234 [44.15%], partial recovery in 119 [22.45%], and no recovery in 150 [28.30%]. 347 [65.47%] patients survived, whereas 153 [28.9%] died during course of hospital stay.
Indian children with AKI commonly had an infectious trigger, high nephrotoxic drug exposure and initial presentation in stage 3(40%). Dialysis was needed in 30%; PD using the stiff catheter was the commonest modality. At discharge only 44% had complete renal recovery. Patient survival was 65%

Acute Kidney Injury (including CKRT)

O-03 - Long-term healthcare utilization and associated costs after childhood dialysis-treated acute kidney injury

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Background: Acute kidney injury (AKI) is common among hospitalized children and is associated with increased hospital length of stay and inpatient costs. However, there are limited data on post-discharge healthcare utilization and costs after AKI hospitalization.
Objectives: To determine long-term healthcare utilization, costs, and physician follow-up patterns after pediatric dialysis-treated AKI hospitalization.
Methods: Using provincial health administrative databases, we performed a retrospective cohort study of all hospitalized pediatric patients (0-18yr) surviving a dialysis-treated AKI episode between 1996-2017 in Ontario, Canada. AKI survivors were matched to four hospitalized comparators without dialysis-treated AKI by age, sex, and admission year. Our primary outcome was post-discharge hospitalizations, emergency department, and outpatient physician visits. We calculated adjusted rate ratios (aRR) using negative binomial regression models. We also evaluated physician follow-up (by specialty) and healthcare costs.
Results: We included 1688 pediatric dialysis-treated AKI survivors and 6752 matched comparators. Dialysis-treated AKI survivors had higher rates of re-hospitalization, emergency department visits, and outpatient physician visits (at 0-1yr, 0-5yr, and 0-10yr; Table). Following adjustment, dialysis-treated AKI survivors had significantly higher rates of re-hospitalization (aRR 1.46 (95% confidence interval (CI) 1.25-1.69, p<0.0001) and outpatient visits (aRR 1.16 (95%CI 1.09-1.23, p=0.01), but not emergency department visits (aRR 1.10 (95%CI 0.99-1.22, p=0.09). Dialysis-treated AKI survivors also had higher healthcare costs *vs.* hospitalized comparators throughout follow-up (median $2549 *vs.* $888 CAD per person-year). Only 18.8% of dialysis-treated AKI survivors had nephrologist follow-up within 1yr post-discharge (Figure), while 92.2% were seen by a family physician or pediatrician in this timeframe. There were no significant differences in post-discharge healthcare utilization or costs between cardiac surgery patients with *vs.* without dialysis-treated AKI.
Conclusions: Dialysis-treated AKI survivors had greater post-discharge healthcare utilization and costs *vs.* hospitalized comparators. Strategies are needed to improve follow-up care for children after dialysis-treated AKI to prevent long-term complications.

Table. Long-term health care utilization and costs among children with dialysis-treated AKI and comparator cohort

Health care utilization	Dialysis-treated AKI n=1,688		Hospitalized comparators n=6,752	
	≥1 visit No. (%)	Events per 1,000 person-years	≥1 visit No. (%)	Events per 1,000 person-years
Hospitalization				
0-1 year	567 (33.6)*	879.3	1,278 (18.9)	432.7
0-10 years	900 (53.3)*	370.5	2,560 (37.9)	205.6
Emergency room visits				
0-1 year	715 (60.8)*	1,758.6	2,433 (51.7)	1,435.8
0-10 years	997 (84.8)*	1,100.2	3,843 (81.7)	930.3
Outpatient physician visits				
0-1 year	1,630 (96.6)*	16,477.1	6,392 (94.7)	10,623.4
0-10 years	1,672 (99.1)	9,829.9	6,697 (99.2)	7,090.3
Health care costs	**Dialysis-treated AKI n=908**		**Hospitalized comparators n=3,632**	
	Median (Q1-Q3) cost/person		**Median (Q1-Q3) cost/person**	
0-1 year	2,594.5 (1,009.0 - 13,921.5)		870.5 (365.0 - 2,637.5)	
0-10 years	10,807.5 (3,494.5 -46,772.0)		3,901.0 (1,542.0 - 11,270.0)	

*p-value <0.05
CAD: Canadian Dollars

Acute Kidney Injury (including CKRT)

O-04 - Persistent markers of renal injury and progressive renal functional decline in children who developed acute kidney injury after surgery for congenital heart disease: A prospective cohort study

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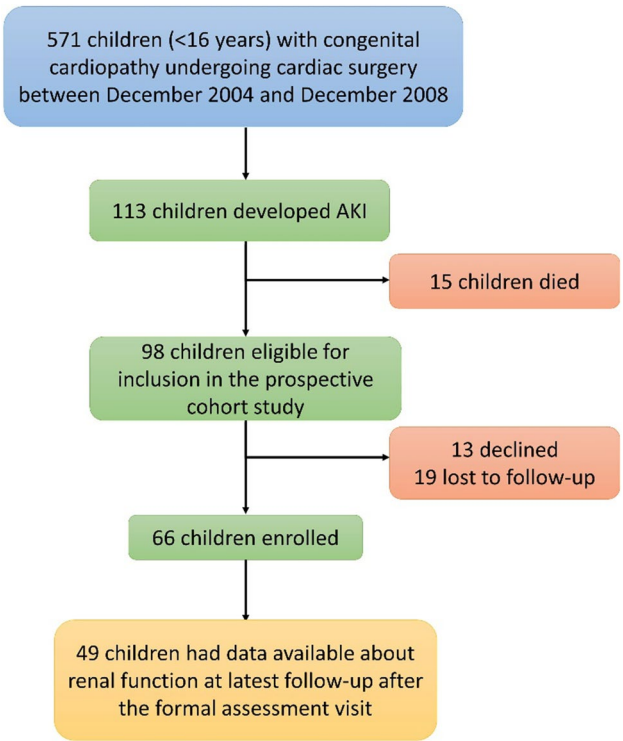
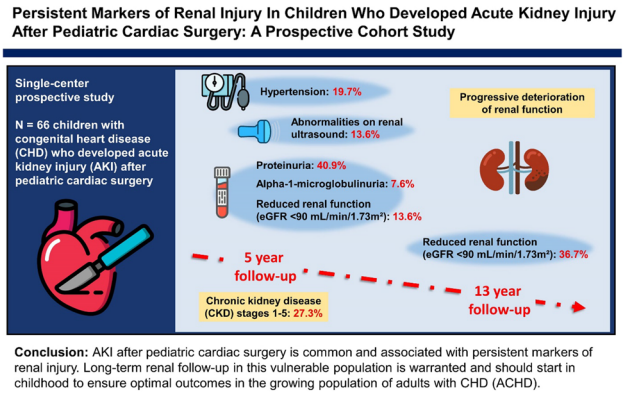
Background: Acute kidney injury (AKI) in the immediate postoperative period is common, occurring in 30-60% of children undergoing pediatric cardiac surgery for congenital heart disease (CHD). Longer-term outcomes and the incidence of chronic kidney disease (CKD) after AKI are not well known. Nonetheless, CKD occurs in up to 30-50% of the growing ACHD population, being responsible for an excess burden in healthcare utilization. This prospective cohort study investigated the renal consequences of AKI at mid- and long-term follow-up.
Methods: All eligible children (<16 years) who had developed AKI following cardiac surgery at our tertiary referral hospital were prospectively invited for a formal renal assessment approximately 5 years after AKI, including measurements of estimated glomerular filtration rate (eGFR), proteinuria, alpha-1-microglobulin, blood pressure, and renal ultrasound. Longer-term follow-up data on renal function were collected at latest available visit.



Results: Among 571 patients operated over a 4-year period, AKI occurred in 113 (19.7%). Fifteen of these (13.3%) died at a median of 31 days (interquartile range, IQR 9-57) after surgery. A total of 66 patients participated in the renal assessment at a median of 4.8 years (IQR 3.9-5.7) after the index AKI episode. Thirty-nine patients (59.1%) had at least one marker of renal injury, including eGFR <90mL/min/1.73m² in 9 (13.6%), proteinuria in 27 (40.9%), alpha-1-microglobinuria in 5 (7.6%), hypertension in 13 (19.7%), and abnormalities on renal ultrasound in 9 (13.6%). CKD stages 1-5 was present in 18 (27.3%). CKD was associated with syndromes (55.6% vs 20.8%, p=0.015). At 13.1 years (IQR 11.2-14.0) follow-up, eGFR <90mL/min/1.73m² was present in 18/49 patients (36.7%), suggesting an average eGFR decline rate of -1.81 mL/min/1.73m² per year.
Conclusions: Children who developed AKI after pediatric cardiac surgery show persistent markers of renal injury. As CKD is a risk factor for cardiovascular comorbidity, long-term renal follow-up in this population is warranted.



Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

O-05 - Impact of HNF1B gene anomalies on renal function decline: a genotype/phenotype correlation study in the European population

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Context: Mutations in Hepatocyte Nuclear Factor 1-Beta (HNF1B), a gene involved in embryonic development, lead to multiorgan developmental disorders and dysfunctions. Clinical manifestations are extremely variable. No clear correlation between genotype and phenotype has been demonstrated hampering disease management.
Objectives: To evaluate the existence of correlations between the type of HNF1B anomaly (deletion versus other anomalies), renal symptoms and loss of GFR.
Methods: Data were obtained from different sources: a survey sent to the members of the European Reference Network for Rare Kidney

Diseases (n=129), a German clinical registry (n=82), a French cohort (n=176) and data collected in our local reference center in Toulouse, France (n=94). From those 491 patients included initially, we excluded 26 patients with a polymorphism or digenism.
Results: 58% of the patients were male subjects. A HNF1B deletion was present in 60% of the patients. Antenatal diagnosis was made in 53% of the cases. 88% of the patients displayed a bilateral ultrasound anomaly. A single functional kidney was observed for 19% due to the presence of unilateral agenesis (2%) or a multicystic dysplastic kidney (17%). The main bilateral ultrasound features were bilateral hyperechogenic kidneys (25%) and/or cortical cystic disease (55%). Isolated renal hypoplasia accounted only for 3%.
In a preliminary analysis involving 324 of the 491 initially recruited patients, 28% of patients developed renal failure as defined by a eGFR <60mL/min/1,73m2. Of those patients developing renal failure, 19% had a HNF1B deletion, while 40% had other HNF1B anomalies ($p<0.05$). No difference between HNF1B deletions or other HNF1B anomalies with respect to the number of functioning kidneys was observed. Finally, the number of functioning kidneys was not associated to the development of CKD.
Conclusions: Our study suggests delayed kidney failure in case of a HNF1B deletion. This could help clinicians to estimate renal prognosis and thus enable individualized counselling.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

O-06 - Constitutive active hedgehog signaling in FOXD1+ embryonic kidney stromal progenitors controls nephron formation via CXCL12 and WNT5A

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[2]*University of Toronto, Laboratory Medicine and Pathobiology, Toronto, Canada*

Background: Low nephron number and expanded renal stroma are hallmark pathologic features of renal dysplasia, the major cause of childhood kidney failure. Yet, lineage-specific mechanisms controlling nephron number are largely undefined. Nephrons and stromal cells arise during embryonic development from *Osr1*-derived *Six2*+ and *Foxd1*+ progenitors, respectively. Given our previous work showing that increased Hedgehog(Hh) signaling in *Osr1*+ cells causes abnormal stromal cell patterning, we sought to define lineage-specific roles for Hh signaling during renal development.
Methods: Human iPSC-derived kidney organoids were treated with the Hh agonist SAG. Constitutive active Hh signaling in *Foxd1*+ stromal cells or *Six2*+ nephron progenitors(NP) was generated in mice by deletion of *Ptch1*, a Hh cell surface receptor, in a *Cre*-dependent manner.
Results: Stimulation of Hh activity in human kidney organoids with SAG(120 nM) resulted in dysplastic tissue characterized by an 88% reduction in WT1+ nephrogenic structures($P<0.01$,n=3) and a 67% reduction in CDH1+ tubular structures($P<0.05$,n=3). SAG-treated organoids also exhibited increased generation of PBX1+ interstitial cells. Mice with *Ptch1*-deficiency restricted to *Six2*+ cells had normal nephron number. In contrast, mice with *Ptch1*-deficiency restricted to *Foxd1*+ stromal progenitors exhibited renal hypodysplasia characterized by a 41% reduction in nephron number($P<0.01$,n=4) and expansion of *Foxd1*-derived PDGFRB+ medullary stromal cells at E18.5, and a 26% reduction in ureteric branch tips at E12.5($P<0.01$,n=6). Complementary bulk and single-cell RNA sequencing of stromal *Ptch1*-deficient mouse kidneys revealed a significant upregulation in stromal *Cxcl12*($P<0.001$,n=3) and *Wnt5a*($P<0.01$,n=3), findings confirmed by RNA microarray analysis of SAG-treated human kidney organoids. Deficiency of *Cxcl12* in *Ptch1*-deficient mice revealed complete rescue of ureteric branching($P<0.001$,n=6) and a 32% rescue in nephron number($P<0.001$,n=4). Deficiency of *Wnt5a* in *Ptch1*-deficient mice similarly generated a 31% rescue of nephron number($P<0.05$,n=3).
Conclusions: Increased stromal *Cxcl12* and *Wnt5a* inhibits formation of a normal number of nephrons, demonstrating the pathogenic actions of dysregulated *Hh-Cxcl12* and *Hh-Wnt5a* signaling.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

O-07 - Long-term outcomes of solitary functioning kidney in children: results from a large multicenter cohort study

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Introduction: A solitary functioning kidney (SFK) in children is a condition that can lead to kidney injury. It is unclear, however, what the long-term risk of kidney injury is and which risk factors are involved. We established a large, nationwide cohort of children with SFK to study the risk of and risk factors for kidney injury in these patients.
Patients and methods: Children with congenital or acquired SFK were recruited in 36 hospitals throughout The Netherlands. Information on potential risk factors for and signs of kidney injury were collected from electronic patient files. Kaplan-Meier models were used to estimate survival without signs of kidney injury and Cox regression analyses were performed to evaluate risk factors.
Results: Detailed clinical information could be obtained for 944 SFK patients with a median age at follow-up of 12.8 years. At the last follow-up measurement, 8% of patients had proteinuria, 33% had an eGFR <90ml/min/1.73m^2, 37% had high blood pressure, and 9% used antihypertensive medication. Survival analyses showed that at 18 years of age, 75% of patients with congenital SFK and 80% of patients with acquired SFK showed at least one sign of kidney injury. Important risk factors included kidney agenesis as cause of the SFK, additional anomalies in the SFK, and being overweight/obese at last follow-up. Kidney agenesis and being overweight/obese were specifically associated with proteinuria and high blood pressure, whereas additional anomalies in the SFK were associated with reduced eGFR.
Conclusions: Many children with SFK will develop kidney injury, stressing the need for long-term follow-up in which lifestyle is an important topic to address. More research into the aetiological background of the risk factors identified will help to translate our findings into individualized care strategies.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

O-08 - A human missense integrin-linked kinase variant negatively regulates murine renal development via mTOR signaling in metanephric mesenchyme

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Nephrogenesis and branching morphogenesis are critical to kidney development and the pathogenesis of Congenital Anomalies of the Kidney and Urinary Tract (CAKUT). Identification of gene variants via genomic sequencing aims to elucidate molecular mechanisms underlying CAKUT. Functional analyses on such variants are required to identify their pathogenic mechanisms. Here, we elucidate pathogenic effects of a CAKUT-associated human missense variant of Integrin-Linked Kinase (ILK), a key regulator of renal branching morphogenesis, on renal development.
An ILK missense variant, *ILK-T173I*, was identified in a CAKUT patient and mother by targeted gene panel sequencing and verified by Sanger sequencing. To begin to identify the molecular pathways downstream of *ILK-T173I*, lentivirus-mediated overexpression of *ILK-T173I* in mouse inner medullary collecting duct (mIMCD3) cells demonstrated dysregulated expression of AKT/mTOR target mRNAs, identified by RNA microarray and qPCR, and elevated levels of phospho-p70-S6Kinase, a mTOR target (n=3, P=0.03). *ILK-T173I* overexpression in mouse embryonic kidneys showed increased phospho-p70-S6Kinase (n=3, P=0.03) and decreased ureteric tip number by 50% (n=15, P=0.003), both of which were rescued by treatment with Rapamycin, an mTOR inhibitor (n=4, P=0.04). Analysis of the pathogenic effects of *ILK-T173I* in a physiologic genetic context was performed in mice in which the *Ilk-WT* allele was replaced with *Ilk-T173I* using CRISPR/Cas9. *Ilk-T173I* knock-in mice were characterized by low nephron number (n=6, P=0.04), decreased ureteric branching (n=5, P=0.006), and increased expression of phospho-p70-s6Kinase (n=3, P=0.014). Treatment of *Ilk-T173I*-knock-in embryonic kidney explants with Rapamycin rescued ureteric branching to levels observed in *Ilk-WT* mice. Unbiased analysis of gene expression by RNA microarray in FAC-sorted ureteric and mesenchymal cell populations isolated from *Ilk-T173I*-knock-in embryonic kidneys indicated elevated mTOR signaling is limited to the mesenchymal cell population.
Together, our data indicate that human Ilk-T173I variant impairs renal development in a mTOR-dependent manner, specifically acting within the mesenchymal cell population.

Ciliopathies (including ARPKD and nephronophthisis)

O-09 - Accuracy of clinical and radiological phenotyping and genetic basis of cystic kidney disease

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[3]*MedGenome Labs Ltd, Bangalore, Karnataka, India*

Introduction: Cystic kidney diseases are chiefly ciliopathies with overlapping clinical and radiological findings and varied genetic defects. Genotype and phenotype are described chiefly for Caucasian patients, and the accuracy of phenotyping and yield of genetic testing are unclear.
Methods: Pediatric patients with cystic kidney disease, diagnosed based on clinical, radiological or histological findings, were enrolled prospectively at a single tertiary care center during 2018-2021. Prespecified clinical and radiological criteria were used to categorize patients as autosomal recessive or dominant polycystic kidney disease (ARPKD, ADPKD), nephronophthisis spectrum of disorders, autosomal dominant tubulointerstitial kidney diseases (ADTKD) and tuberous sclerosis complex (TSC). Variants on clinical or whole exome sequencing, performed in a subgroup of patients, were categorised using ACMG 2015 criteria.
Results: Of 186 patients with suspected cystic kidneys, 122 patients (115 families) were phenotyped as nephronophthisis-spectrum disorders (n=62), ARPKD (n=26), ADPKD (n=18), TSC (n=11), and ADTKD (n=5). Causative variants (n=63) were detected in 58 (71.6%) of 81 patients who underwent genetic testing (Table 1). Pathogenic (n=29) or likely pathogenic (n=18) variants and variants of uncertain significance (n=16) were inherited in homozygous (n=17), compound heterozygous (n=20) or heterozygous (n=31) manner; 37 variants were novel. Genetic testing confirmed the diagnosis in 46 (56.8%) patients, including 86% of 13 patients with ADPKD, 67% of 15 with ARPKD, 46% of 27 with nephronophthisis, 88% of 9 with TSC, and 80% of 5 patients with ADTKD. Twelve (14.8%) patients had phenocopies, indicating inaccurate clinico-radiological classification, most often with nephronophthisis.
Conclusions: Exome-sequencing established the diagnosis in 71.6% [95% CI 61.1-80.6%] of pediatric cystic kidney diseases. Clinico-radiological phenotyping was inaccurate in one-sixth cases, chiefly nephronophthisis. The yield of testing was highest for TSC and ADPKD and low for nephronophthisis.

Table 1. Significant variations on genetic testing (n=81)

Phenotype (n diagnosed/tested)	Gene	ACMG category (n)	Exon: Codon change; protein change	Zygosity	Reported
ADPKD (11/13)[#1]	*PKD1*	Pathogenic (9)	11:c.2249G>A; p.Trp750Ter 21:c.7948_7949del; p.Leu2650GlyfsTer10 37:c.10842C>G; p.Tyr3614Ter 40:c.11401dup; p.Asp3801GlyfsTer15 Intron39:c.11269+1G>A 40:c.11317_11363dup; p.His3789GlnfsTer53 Intron43:c.12004-1G>T 44:c.12010del, p.Gln4004SerfsTer35 45:c.12390-12391delinsTT; p.Glu4131Ter	Het Het Het Het Het Het Het Het Het Het	No No No No No Yes No Yes Yes Yes
		Likely pathogenic (2)	38:c.11045T>G; p.Leu3682Arg 46:c.12449G>C; p.Arg4150Pro	Het Het	No No
ARPKD (10/15)[#2]	*PHKD1*	Pathogenic (2)	60:c.10156G>T; p.Gly3386Cys 63:c.11314C>T; p.Arg3772Ter	C Het C Het (2)	No Yes
		Likely pathogenic (5)	3:c.107C>T; p.T36M 32: c.4811C>T; p.Thr1604Met 16:c.1260del; p.Thr421LeufsTer41 32:c.4870C>T; p.Arg1624Trp 30:c.3467C>T; p.Ser1156Leu	Homo Homo (2) C Het C Het (2) C Het	Yes Yes No Yes No
		VUS (6)	32:c.5213_5215del;p.Ile1738de 38:c.6146C>T; p.Thr2049Ile 17:c.1589C>A; p.Ala530Asp 39:c.6427G>A; p.Gly2143Arg 57:c.8915G>T; p.Gly2972Val 22:c.2167C>T; p.Arg723Cys	Homo C Het C Het C Het C Het C Het	No No No No No No
Nephronophthisis spectrum (13/27)[#3]	*NPHP1* *NPHP1* *INVS* *NPHP3* *NPHP3* *NPHP4* *NPHP4* *IQCB1* *BBS7*	Pathogenic (9)	Deletion of all exons Deletion 1-10 exons 16:c.3062_3063del,p.Lys1021SerfsTer20 INV513:c.1985+5G>A 18:c.2563C>T;p.Gln855Ter 10:c.1148_1149delinsGCC, p.Leu383ArgfsTer19 18:c.2380del, p.Asp794ThrfsTer5 13:c.1363C>T, p.Arg455Ter 4:c.297C>T; P.Gln99Ter	Homo (2) Homo Homo Homo C Het Homo Homo Homo C het	Yes Yes No Yes Yes No No Yes No
	CEP290	Likely pathogenic (1)	54:c.7394_7395del; p.Glu2465ValfsTer2	C Het	No
	NPHP3 *BBS7* *AHI1* *CSPP1* *BBS5*	VUS (5)	Intron 15:c.21171+136A>G 7:c.619C>T, p.Leu207Phe 14:c.2039T>C, p.Leu207Phe 28:c.3389T>G, p.Leu1130Arg 16:c.1526A>G, p.Tyr509Cys	C Het C.Het Homo Homo C Het	No No No No No
Tuberous sclerosis (8/9)	*TSC2*	Pathogenic (3)	11:c.1060C>T; p.Gln354Ter Intron15:c.1599+1G>A 41:c.5227C>T; p.Arg1743Trp	Het Het Het	Yes Yes Yes
		Likely pathogenic (3)	37:c.4849G>C; p.Ala1617Pro 4-9:c.(336+1_337-1)_(848+1_849-1)del 1-4: g.(_2043567)_(2053452_)del	Het Het Het	Yes Yes Yes
	TSC2-PKD1	Likely pathogenic (2)	PKD1 exon 46 and TSC 1-42 deletion Chr16:g.(2062497_2062600)_(2117791_2118462)del	Het Het	Yes Yes
ADTKD (4/5)	*HNF1B*	Pathogenic (3)	2:c.544C>T; p.Q182* Intron 4: c.1046-2A>G 3:c.655_677del; p.Ser219HisfsTer67	Het Het Het	Yes Yes No
	17q12	Likely pathogenic (1)	Chr17:g.(_36486700)_(37744884)del	Het	Yes

*Clinical- and whole-exome sequencing in 42 and 36 patients, respectively; 3 siblings were diagnosed on Sanger sequencing; [#]Phenocopies included one patient each with [1]apparent mineralocorticoid excess (*HSD11B2*); [2]HNF1B-nephropathy (*17q12* microdeletion); [3]three with HNF1B-nephropathy (two with *HNF1B* variants; one with *17q12* microdeletion), three with *PAX2*-related renal hypodysplasia (two with *PAX2* variation; one with *10q* microdeletion), and one case each with bile acid synthesis defect (*CYP7B1*), Gitelman (*SLC12A3*) and Alport (*COL4A5*) syndromes, and Fanconi anemia (*ERCC4*); VUS variant of uncertain significance

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

O-10 - High phosphate diet causes left ventricular dilatation and cardiomyocyte hypercontractiliy in mice

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Objectives: Hyperphosphatemia and elevated levels of the phosphaturic hormones fibroblast growth factor 23 (FGF23) and parathyroid hormone (PTH) are associated with increased cardiovascular risk in patients with chronic kidney disease. Whether a chronic oral phosphate loading impacts on cardiac health *per se* is unknown.
Methods: Male C57BL/6 mice received a 2% high phosphate diet (HPD) or a 0.8% normal phosphate diet (NPD) for six months. Cardiac function was assessed by echocardiography and Millar catheter, and bulk RNA sequencing (RNAseq) was performed in total heart tissue. Calcium signaling and contractility were assessed in isolated adult mouse cardiomyocytes (AMCM) form mice on NPD and HPD *ex vivo*.
Results: HPD resulted in increased FGF23, PTH and phosphate levels, and hyperphosphaturia which was associated with slowly progressive kidney disease. Mice on HPD showed a dilatated left ventricle (LV) with reduced anterior and posterior wall thicknesses and enhanced LV diameters and volumes during systole and diastole. Ejection fraction and fractional shortening were significantly reduced in HPD-fed mice indicating impaired systolic function. Moreover, LV end-systolic pressure was higher in HPD mice. Contractility measurements of AMCMs from HPD-fed mice showed a significantly higher shortening velocity, increased shortening amplitude and percent sarcomere shortening, and a faster relaxation compared to AMCMs from NPD controls. The latter was associated with faster calcium reuptake shown by significantly shorter time to baseline 90% of calcium and decreased Tau. RNAseq analysis revealed significant changes in the expressions of genes involved in calcium signaling suggesting that HPD impaired calcium signaling contributed to the observed cardiac phenotype in HPD mice.
Conclusions: High dietary phosphate intake alters phosphate metabolism and induces LV dilatation with reduced systolic function *in vivo* which is associated with cardiomyocyte hypercontractiliy *ex vivo* characterized by faster relaxation and Ca^{2+} reuptake into the sarcoplasmic reticulum after contraction.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

O-11 - Urinary DKK3 predicts short-term eGFR decline and nephroprotective efficacy of antihypertensive therapy in children with CKD: Findings from the 4C Study and ESCAPE Trial

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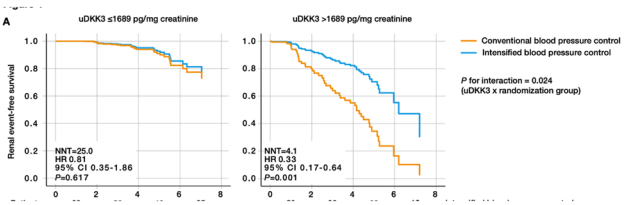
Background: Childhood-onset chronic kidney disease (CKD) is a progressive condition with major impact on life expectancy and quality. We identified urinary Dickkopf-3 (uDKK3) as a marker of renal tubular cell stress. Here, we evaluated the usefulness of uDKK3 in determining the short-term risk of CKD progression in children and identifying those who will benefit from specific nephroprotective interventions.
Methods: The association between uDKK3 and semi-annual eGFR decline, and its interaction with intensified blood pressure reduction in the ESCAPE Trial was assessed. Estimated glomerular filtration rate (eGFR) and uDKK3 were quantified in 659 children with CKD enrolled in the multicenter ESCAPE and 4C studies at baseline and at 6-monthly follow-up visits, yielding 4,030 semi-annual evaluation blocks.
Results: In the randomized-controlled ESCAPE trial, the effect of intensified blood pressure control on the renal survival endpoint and the need for renal replacement therapy was limited to children with uDKK3 above the median, i.e. >1,689 pg/mg creatinine (HR 0.33, 95%CI: 0.17-0.64; NNT 4.1 vs. 25.0 and HR 0.27, 95%CI: 0.11 to 0.66; NNT 6.7 vs. 55.6). In both cohorts, uDKK3 >1,689 pg/mg was associated with significantly greater 6-month eGFR decline (-6.3%, 95%CI: -7.8 to -4.9% vs. 0.2%, 95%CI:-1.1 to 1.6%, P=4.2x10^{-10} in ESCAPE, and -6.5%, 95%CI:-13.4 to -0.4 vs. -1.7%, 95%CI:-8.6 to 5.2, P=2.4x10^{-10} in 4C), independently of renal diagnosis, eGFR, and albuminuria.
Conclusions: uDKK3 is associated with a greater short-term risk of declining kidney function and may allow a personalized medicine approach to pharmacological nephroprotection by identifying children who benefit from intensified blood pressure lowering.



Paediatric nephrology in under-resourced areas

O-12 - Pediatric nephrology resources in low and middle income (LMI) countries: a survey from the IPNA Priorities in Low Resource Countries Committee (LRCC)

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Background: The IPNA LRCC seeks to define needs and improve pediatric nephrology care in LMI countries. In 2021, a comprehensive online survey eliciting information in the areas of human resources, diagnostics, and therapeutics was distributed to pediatric centres through IPNA and regional organisational contacts. Initial survey analysis is presented herein.
Results: Responses were received from 247 centres in 62 LMI countries representing 84.2% of the global LMI population. Of these centres, 34% were university/medical school affiliated, 66% were government funded, 13.4% were privately funded, and 6.1% received support from a trust/charitable organisation. Pediatric nephrologists staffed 94.3%, and general pediatricians provided care at 5.3% of these centres. Adult nephrologists provided support in 38% of centres with pediatricians only. Pathologists, radiologists, pediatric surgeons, and PICU were present at 78.3%, 93.5%, 92%, and 85% of the centres respectively. Dietitians were available at 78.2% of centres.
In-house laboratories were available at 83.2% of sites. Urine dipstick, microscopy, culture and sensitivity is performed at >94% of centres. Renal function tests were available at 99.1% and complement testing at 80.6% of sites. Renal biopsy was performed in 83.2% with histopathology available at 67.8% and immunofluorescence at 55.1% of centres. Ultrasound was widely available (99.1%) and voiding cystourethrogram at 86.7% of centres. Patients' inability to pay limited access to diagnostics at 30.8% of centres.
Therapies available included acute peritoneal dialysis (85%), acute hemodialysis (82.8%), chronic peritoneal dialysis (64.3%), chronic hemodialysis (67.8%), and renal transplantation in 34.3% of centres. Access to common medications in pediatric nephrology was assessed (Table 1).

Table 1: Availability of commonly used medications in pediatric nephrology

	Responses, *n*	Medication Available, *n(%)*	Difficult to obtain, *n(%)*	Limited by Patient Finances, *n(%)*
Prednisone	191	187(97.9)	18(9.4)	50(26.2)
Methylprednisolone	190	179(94.2)	25(13.2)	57(30)
Cyclophosphamide	188	138(73.4)	22(11.7)	62(33)
Cyclosporine	185	148(80)	31(16.8)	69(37.3)
Tacrolimus	183	137(74.9)	26(14.2)	68(37.2)
Mycophenolate	185	145(78.4)	30(16.2)	73(39.5)
Short Acting ACEI	186	156(83.9)	12(6.5)	45(24.2)
Long Acting ACEI	187	175(93.6)	14(7.5)	46(24.6)
Short Acting CCB	187	168(89.8)	11(5.9)	41(21.9)
Long Acting CCB	188	171(91)	18(9.6)	43(22.9)
20-25% Albumin	187	174(93)	30(16)	73(39)
Furosemide	186	183(98.4)	12(6.5)	41(22)
TMP/SMX	185	170(91.9)	15(8.1)	39(21.1)

ACEI=angiotensin converting enzyme inhibitor; CCB=calcium channel blocker; TMP/SMX=trimethoprim/sulfamethoxazole

Conclusion: While most LMI centres had basic pediatric nephrology services, there was a limited availability of renal pathology, chronic dialysis and renal transplantation services. Patient finances were a barrier to accessing diagnostic and therapeutic resources. Further analysis focusing on geographic variability will serve to guide LRCC efforts.

Paediatric nephrology in under-resourced areas

O-13 - Caloric restriction during pregnancy impairs nephrogenesis by modifying epigenetic regulation in nephron progenitor cells

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Introduction: Poor intrauterine environment, such as maternal malnutrition, impairs nephron endowment and increases the risk of chronic kidney disease in adulthood in the next generation. We have previously demonstrated that methionine metabolism has an important role in mediating the negative effects of caloric restriction during pregnancy on nephron endowment. As methionine has an important role in epigenetic control of gene expression, we examined the effects of malnutrition on gene methylation in nephron progenitor cells.
Methods: Caloric intake of pregnant mice was limited to 70% of daily intake. Nephron progenitor cells were sorted using transgenic mice with specific GFP labeling. DNA from nephron progenitors was extracted and methylation pattern was characterized and analyzed using reduced representation bisulfite sequencing. The data acquired was cross-referenced with expression data from RNA-sequencing of nephron progenitor cells under caloric restriction and validated using RT-qPCR. The effects of methionine on methylation patterns were evaluated using Bisulfite Amplicon Sequencing.
Results: Caloric restriction during pregnancy leads to a global decrease in DNA methylation in nephron progenitor cells, compared to control. Specific changes in DNA methylation were localized to gene promoters, enhancers and transcription factor binding sites. These were present throughout the genome, including genes involved in nephrogenesis and pivotal intracellular signaling pathways, in accordance with the changes in expression profile.
Conclusions: This is the first evidence that maternal malnutrition during pregnancy impairs nephrogenesis by modifying epigenetic remodeling in nephron progenitor cells, presumably mediated by methionine.

Paediatric nephrology in under-resourced areas

O-14 - Comparison of Darbepoetin alpha and recombinant Human Erythropoietin for treatment of anemia in pediatric chronic kidney disease patients: A non-inferiority trial

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Background: Darbepoetin alfa (DA) is a long-acting erythropoiesis stimulating agent with a two-to-four fold longer half-life compared to recombinant human erythropoietin (rHuEPO) in both adults and children. The aim of this study was todetermine whether or not DA was non-inferior to rHuEPO in the treatment of anemia in children with chronic kidney disease (CKD) stage 3-5 (on or not on dialysis).
Methods: Fifty patients of either gender (aged 1-18 years) with CKD stage 3-5 (on or not on dialysis) who had baseline hemoglobin (Hb) between 9-12 g/dL and were on stable erythropoietin therapy for at least 8 weeks were randomized (1:1) to either continue rHuEPO or switch to DA therapy for a period of 28 weeks. Doses were titrated in the initial 23 weeks to maintain the Hb between 11-12 g/dL and efficacy was assessed between week 24-28. The primary efficacy endpoint was the mean change in Hb between baseline and the evaluation period.
Results: In the intention-to-treat population (n = 50), the adjusted between group difference in mean Hb change between the baseline

and the evaluation period was 0.131 g/dL (95% CI: –0.439 to 0.719, p=0.629). The lower limit of the two-sided 95% CI for the difference in the mean change in Hb between the two treatment groups was well above the pre-specified non-inferiority margin of − 1.0 g/dL (Table 1)

Table 1: Mean change in hemoglobin between the baseline and the evaluation period using ANCOVA model adjusted for covariates.

Statistics	PP Population		ITT Population	
	rHuEpo (n-20)	DA (n-23)	rHuEpo (n-24)	DA (n-26)
Baseline Hb (g/dl), mean (SD)	9.59 (0.61)	9.517(0.38)	9.571 (0.586)	9.485 (0.377)
Final Hb (g/dl), mean (SD)	11.0 (0.84)	11.165 (0.96)	10.871(0.898)	10.98 (1.054)
Within group comparison:				
Mean change from baseline* (g/dl)	1.438	1.619	1.341	1.481
SE* (g/dl)	0.208	0.194	0.204	0.195
95% CI* (g/dl)	1.016, 1.859	1.228, 2.011	0.931, 1.751	1.088, 1.875
P value	0.000	0.000	0.000	0.000
Between group comparison:				
Mean change from baseline* (g/dl)	0.182		0.131	
SE* (g/dl)	0.293		0.283	
95% CI* (g/dl)	-0.410, 0.774		-0.439, 0.719	
P value	0.538		0.629	

CI confidence interval, DA Darbepoetin alpha, Hb hemoglobin, rHuEpo recombinant human erythropoietin, SE standard error
* Figures reported after adjusting for age and baseline Hb

Similar pattern of non inferiority was seen for per protocol population. The safety profile of DA and rHuEPO were also comparable with injection site pain being the only reported side effect.
Conclusion: DA is non-inferior to rHuEPO for the treatment of anemia of CKD in pediatric population with a comparable safety profile.

Haemodialysis and peritoneal dialysis

O-15 - Modifiable predictors of blood pressure control in pediatric hemodialysis patients – can we do it better? Results from the International Pediatric Hemodialysis Network (IPHN)

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[9]*CHU Arnaud de Villeneuve, Pediatric Neprology, Montpellier, France*
[10]*University Hospital Motol, Pediatric Neprology, Prague, Czech Republic*
[11]*Dialysis Division for Children, Pediatric Neprology, Zabrze, Poland*
[12]*The University of California- San Francisco UCSF, Pediatric Neprology, San Francisco, USA*
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[14]*Center for Pediatrics and Adolescent Medicine, Pediatric Neprology, Heidelberg, Germany*

Introduction: Fluid and salt overload in dialysis patients result in high blood pressure (BP), left ventricular hypertrophy (LVH) and are associated with poor outcome. Knowledge on modifiable factors in pediatric hemodialysis patients is limited.
Methods: 954 pediatric hemodialysis (HD) patients (542 boys /412 girls), aged 0 to 21 (median 12) years on chronic HD(F), treated at 65 pediatric dialysis units in 30 countries were prospectively followed by the IPHN.
Results: In 2838 6-monthly observations 28% of patients were normotensive without antihypertensives, while 17% were normotensive on 2.1±1.0 antihypertensives; 55% of the patients were hypertensive. 24% of HD and 33% of HDF patients were normotensive without treatment (p<0.001). Systolic BP-SDS was independently predicted (PE±SEM) by inter-dialytic weight gain (IDWG; 0.22±0.49, p>0.0001), younger age (-0.07±0.01, p<0.0001) and dialysate calcium (0.48±0.16, p=0.006), while diastolic BP-SDS was predicted by younger age (-0.06±0.001, p<0.0001), dialysate calcium (0.63±0.15) and dialysate sodium (0.06±0.01; p=0.01). Dialysis modality, urine output, weekly dialysis time and ultrafiltration rate were not predictive. Presence of hypertension (systolic and/or diastolic SDS≥1.645) was independently associated with IDWG (OR 1.31, CI 1.15-1.48, p<0.0001), younger age (OR 0.93 CI 0.92-0.96, p<0.0001), dialysate calcium (OR 1.9, CI 1.25-2.86, p=0.0002) and HD modality (OR for HD 1.31, CI 1.07-1.59; p=0.008). Intradialytic hypotension was reported in 23% of dialysis sessions and it was independently (PE±SEM) predicted by higher IDWG (0.88±0.15, p<0.0001), HD vs. HDF (2.2±0.71, p=0.002), younger age (-0.10±0.006, p=0.004) and lower dialysate calcium (-3.81±1.45, p=0.01).
Conclusions: High blood pressure is still prevalent in the majority of hemodialysis patients despite elaborated antihypertensive therapy in the majority of them. Predictive and modifiable factors of BP include IDWG, dialysis modality, dialysate sodium and dialysate calcium, with the latter, however, inversely impacting on the risk of intradialytic hypotension. HDF is associated with better BP control and hemodynamic stability.

Genetics and Genetic Disease (not otherwise more specifically categorised)

O-16 - The regulation of the nephrin-nephrin distance by podocin mediates the interallelic interactions of the NPHS2 R229Q variant

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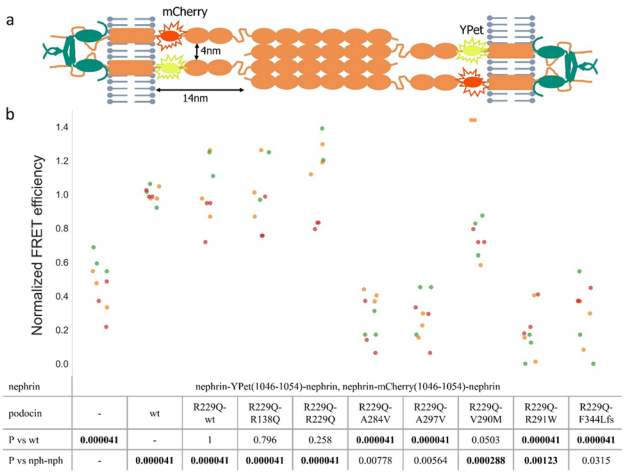
Background: *NPHS2* is the most frequently mutated gene in podocytopathies. We formerly showed that its R229Q variant is only pathogenic when associated to specific 3' mutations in trans. The encoded podocin homooligomerizes through its C-terminal and binds nephrin in the slit diaphragm. We formerly explained the interallelic interactions of R229Q podocin by an altered oligomerization which causes altered trafficking. However, this contrasted the mild course of the associated renal failure. We recently showed that podocin decreases the distance between the nephrin molecules. Unexpectedly, we also found that abnormal podocin oligomers become membranous in the presence of nephrin. We therefore hypothesized that the pathogenic R229Q oligomers are unable to diminish the nephrin-nephrin distance.
Method: HEK293 cells were transfected with a single vector encoding one (pLEX-MCS) or two (pKK-BI16) podocin variants and two vectors (pEGFP-N1) encoding different nephrin constructs tagged either with YPet or mCherry replacing the extracellular fibronectin domain. FRET efficiency was measured between YPet and mCherry in living HEK293 cells, 48h after transfection. Measurements were repeated nine times in three experiments.
Results: While all benign podocin variants/associations (wt, R229Q, R229Q-wt, R229Q-R138Q, R229Q-V290M) increased the FRET efficiency (decreased the distance) between the nephrin molecules, none of the pathogenic variants/associations (R138Q, A284V, R286Tfs, V290M, R229Q-A248V, R229Q-A297V, R229Q-F344Lfs, R229Q-R291W) exerted such an effect (Figure 1). Not only was there a highly significant difference in the FRET efficiency between the benign and the pathogenic variants/associations ($p = 1.19x10^{-33}$), but a cut-off value could distinguish them in 97% of the measurements.

Figure 1: FRET measurements between nephrin molecules in the presence of benign and pathogenic podocin oligomers



nephrin		nephrin-YPet(1046-1054)-nephrin, nephrin-mCherry(1046-1054)-nephrin								
podocin	-	wt	R229Q-wt	R229Q-R138Q	R229Q-R229Q	R229Q-A284V	R229Q-A297V	R229Q-V290M	R229Q-R291W	R229Q-F344Lfs
P vs wt	**0.000041**	-	1	0.796	0.258	**0.000041**	**0.000041**	0.0503	**0.000041**	**0.000041**
P vs nph-nph	-	**0.000041**	**0.000041**	**0.000041**	**0.000041**	0.00778	0.00564	**0.000288**	**0.00123**	0.0315

a) Schematic diagram of the nephrin constructions with juxtamembranous YPet and mCherry labeling, replacing the E1046-P1054 residues of nephrin (modified after the works of Ruotsalainen et al., 1999; Straner et al., 2018).
b) Normalized FRET efficiency values measured between Ypet- and mCherry-tagged nephrin molecules in function of the coexpressed podocin variants. Values obtained from the same experiment are shown in the same color. Significant P values are in bold (p<0.0029).

Conclusion: Pathogenic podocin oligomers are unable to decrease the distance between the nephrin molecules: the shortest dimension of the glomerular pore. This mechanism explains the molecular basis of the first clinically relevant interallelic interactions in human genetics, and the milder disease course. This method can help evaluating the pathogenicity of novel R229Q interactions.

Genetics and Genetic Disease (not otherwise more specifically categorised)

O-17 - The potential of CTNS-mRNA based gene replacement therapy to treat nephropathic cystinosis

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Background and Objectives: Cystinosis is an autosomal recessive lysosomal storage disorder caused by mutations in the *CTNS* gene, encoding cystine transporter cystinosin. Mutations result in lysosomal cystine accumulation in all cells of the body with kidney being the most affected organ. The current standard therapy, cysteamine, reduces cellular cystine levels, but does not cure renal Fanconi syndrome (a generalized proximal tubular dysfunction).
mRNA has revolutionized the world of molecular therapy and mRNA-based therapeutics have started to emerge in the kidney field**.** Our aim is to investigate mRNA-based gene replacement to treat cystinosis.
Methods: Patient derived proximal tubular epithelial cells (PTECs) were transfected with synthetic *CTNS*-mRNA. A HA-tag was included in the mRNA-sequence, allowing immunostaining. Transfection efficiency, protein expression over time and localisation was studied by immunofluorescence staining for the HA-tag and the lysosomal associated membrane protein 1 (LAMP1). At specific time points cystine measurement was performed to assess the short- and long-term effect of a single *CTNS* mRNA dose.
Results: PTECs were evaluated for the expression of cystinosin from 12h to 10 days post-transfection. Transfection efficiency was 78% ±12% for 48h with no protein being detectable after 4 days. Co-staining with LAMP1 confirmed the lysosomal localisation at 24h post-transfection. Furthermore, the functionality of the *CTNS*-mRNA was evaluated by cystine measurement and showed a 50% decrease in cystine content 24h after treatment that persisted up to 7 days (Figure 1).
Conclusion: Our results show that mRNA-based gene replacement results in lysosomal cystinosin expression in cystinotic cells for 4 days and leads to significant cystine reduction that lasts at least 7 days.

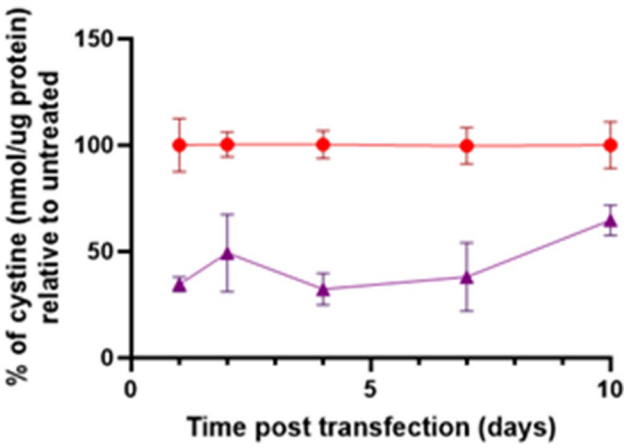

Figure 1: Reduced cystine levels persist for up to 7 days post-transfection of cystinotic PTECs with 500ng/ml CTNS-3HA mRNA (purple). A gradual increase occurs at 10 days. Cystine levels (mean ± SD) were normalized to total protein and the untreated control (red).

Genetics and Genetic Disease (not otherwise more specifically categorised)

O-18 - Investigating the role of the complement system in paediatric sickle cell disease

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Introduction: Sickle cell disease (SCD) is one of the most common hereditary red blood cell (RBC) disorders, with an estimated 300,000 infants born worldwide with the disease annually. In SCD, a mutation in the gene for β-globin results in rigid sickled RBCs that can form blockages in the micro-vessels within organs, such as the kidney, leading to intravascular RBC lysis, endothelial cell (EC) damage, ischemia/reperfusion injury, and extremely painful vaso-occlusive crises (VOC). SCD can give rise to a variety of renal manifestations such as hyperfiltration, microalbuminuria, and acute kidney injury. Approximately 16-18% of overall mortality in patients with SCD is ascribed to kidney disease. The complement system – a critical part of innate immunity – is involved in an increasing number of kidney and vascular disorders, with emerging research pointing to the involvement of complement in SCD.
Aim: To determine the contribution of complement to SCD and sickle cell nephropathy (SCN) using a cohort of paediatric SCD patients.
Methods: Paediatric patients with SCD (HbSS or HbS/β0) were enrolled in the study during hospital admission with diagnosed VOC or acute chest syndrome (ACS) not suspected to be caused by infection. Patient serum and plasma was collected during hospital admission (crisis) and during follow-up appointments (baseline), and stored at -80 °C until analysis. Classical pathway, mannose-binding lectin (MBL) pathway, and alternative pathway complement activity was measured using the WIESLAB Complement System Screen (Svar Life Science).
Results: Preliminary data suggests that, different from the classical and alternative pathways, there is an interesting trend in the MBL pathway between baseline and crisis patients.
Conclusion: This study aims to establish a new link between complement and EC injury in SCD. Future experiments will focus on further quantifying complement levels in patient serum, and assessing the biological consequences of this on the surface of endothelial cells.

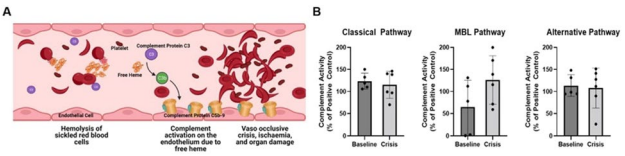

Figure 1. A) Extended model of sickle cell disease pathogenesis highlighting complement system and endothelial cell activation, contributing to vaso-occlusive crisis. **B)** Different from the classical and alternative pathway, the MBL pathway shows an interesting trend between patients at baseline (n=5) and crisis (n=6).

Genetics and Genetic Disease (not otherwise more specifically categorised)

O-19 - Effects of burosumab treatment on mineral homeostasis in children and adolescents with X-linked hypophosphatemia: lessons from the German XLH Registry

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Introduction: Burosumab was approved for treatment of pediatric patients with X-linked hypophosphatemia (XLH). However, data on its efficacy in adolescents (age > 12 years) and in real-world settings are lacking.

Material and methods: Here we assess the effects of 12 months burosumab treatment on mineral homeostasis in 77 pediatric XLH patients (50 children, 27 adolescents) enrolled in the German XLH Registry. Age and sex related SD scores (SDS) were calculated for serum phosphate and alkaline phosphatase (ALP) levels, and renal tubular reabsorption of phosphate per glomerular filtration rate (TmP/GFR).
Results: At baseline, all patients presented with profound hypophosphatemia (-4.5 SDS), reduced TmP/GFR (-6.5 SDS), and elevated ALP (2.7 SDS, each $p<0.001$ versus healthy children) suggesting persisting rickets despite long-term therapy with oral phosphate and active vitamin D. Burosumab treatment resulted in rapid increases in mean serum phosphate and TmP/GFR by approx. 0.3 mmol/l amounting to -2.2 SDS and -2.5 SDS at 12 months, respectively (each $p<0.001$ versus baseline). This was paralleled by a continuous decrease in serum ALP (1.3 SDS, $p<0.001$ versus baseline). Serum phosphate, TmP/GFR, and ALP values were normalized in approximately 40%, 30% and 80% of patients, respectively. Two patients had transient hyperphosphatemia due to a dosing error. At 12 months, the median burosumab dosage amounted to 0.8 mg/kg (range 0.6-1.2). Serum phosphate levels at 12 months were comparable between children (-2.3 SDS) and adolescents (-2.1 SDS) and associated with parathyroid hormone (PTH) levels. Serum ALP z-scores were associated with PTH levels in adolescents but not in children.
Conclusions: In this real world setting 12 months burosumab treatment was effective to normalize serum ALP levels in children and adolescents with XLH suggesting healing of rickets despite persisting mild hypophosphatemia in about half of patients. Elevated PTH levels are a risk factor for failure to normalize mineral homeostasis.

Genetics and Genetic Disease (not otherwise more specifically categorised)

O-20 - Renal and extra-renal outcome of siblings with infantile nephropathic cystinosis treated with cysteamine from symptomatic versus presymptomatic age: A multicentric sibling cohort study

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Background and objectives: Infantile Nephropathic cystinosis (INC) is an inheritable lysosomal storage disorder characterized by lysosomal cystine accumulation, progressive chronic kidney disease and multiple extra-renal complications. Cysteamine postpones the onset of end-stage kidney disease (ESKD) and reduces the incidence of extra-renal complications. However, the effect of the cystinosis genotype on the extra-renal outcome, and of initiation of cysteamine therapy in the presymptomatic versus symptomatic phase, remain to be elucidated.
Design, setting, participants, and measurements: An international multi-centric retrospective cohort study of pairs of INC index patients with corresponding siblings was set up via collaboration of thirteen European Cystinosis reference centers in order to study their outcome.
Results: Twenty-seven pairs of INC index and sibling patients were recruited, comprising 17 pairs of symptomatic diagnosed siblings with corresponding index patients, and 10 pairs of presymptomatic diagnosed siblings with corresponding index patients. Symptomatic siblings were initiated on cysteamine treatment about 15 months earlier, and reached ESKD at a significant later age compared to their index counterparts. With an average age at last observation of 10 ± 6 years, none of the presymptomatic diagnosed siblings treated from neonatal age have reached ESKD yet. No significant difference in the number of extra-renal complications was observed between siblings and their corresponding index patients. While the age at introduction of cysteamine was a determining factor for both renal and extra-renal outcomes, in this cohort we could not demonstrate the cystinosis genotype being an independent significant predictor for the extra-renal outcome.
Conclusions: In INC, while the age at initiation of cysteamine affects both the renal and extra-renal outcomes, the cystinosis genotype has no significant impact on either outcome. Importantly, initiation of cysteamine treatment at neonatal age is associated with a superior renal outcome supporting the inclusion of cystinosis in newborn screening programs.

Hypertension

O-21 - Change in blood pressure classifications after the 2017 Clinical Practice Guideline in youth referred for hypertension: interim results from the Study of the Epidemiology of Pediatric Hypertension (SUPERHERO) Registry

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Background: In 2017, the American Academy of Pediatrics released the Clinical Practice Guideline (CPG) for hypertension (HTN) in children and adolescents. Compared to the prior Fourth Report in 2004, the CPG updated normative blood pressure (BP) data and thresholds to classify HTN.

Objective: Our objective was to study whether the proportion of youth with HTN at the initial clinic visit changed after the CPG.
Methods: The Study of the Epidemiology of Pediatric Hypertension (SUPERHERO) Registry is an ongoing international multicenter retrospective cohort of youth referred to subspecialty care for HTN disorders. EHR data are collected with validated bioinformatics scripts. Inclusion criteria are ICD-10 code-identified HTN disorder from 1/1/2016–12/31/2021 and age <19 years at baseline. Exclusion criteria are pregnancy, kidney failure on dialysis, or kidney transplant. We further excluded participants <1 year of age and those missing BP data. We analyzed data from the baseline visit. Fourth Report criteria were applied up to 12/31/2017, while the CPG criteria were applied starting 1/1/2018. We tested for trends across time using linear regression, Jonckheere-Terpstra test, Cochran-Armitage trend test, and Cochran-Mantel-Haenszel test and between-group comparisons with chi-square test.
Results: Of the 3097 youth included (median age 14.5 years, 37% females), 38% were in the Fourth Report era (2016-2017) and 62% were in the CPG era (2018-2021). Median age decreased over time while obesity prevalence increased over time. The proportion of participants with a baseline BP classified as HTN increased significantly from the Fourth Report era to the CPG era (47% to 64%, $p<0.05$) (Figure).
Conclusions: The introduction of the American Academy of Pediatrics CPG in 2017 was associated with a higher proportion of HTN at the baseline subspecialist clinic visit. Ongoing analyses will better define the pattern of these changes and further elucidate the underlying reasons.

Hypertension

O-22 - Temporal trends in prevalence of blood pressure screening and hypertension after introduction of clinical practice guidelines on hypertension in Canadian children: A time-series analysis

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Background/Objectives: In 2016 & 2017 respectively, new Canadian & American guidelines for assessing pediatric hypertension (HTN) were introduced. Our main objectives were to determine whether these guidelines have impacted HTN prevalence as well as blood pressure (BP) screening patterns in Canadian primary care settings.
Methods: The study included 438,297 children (3-18 years) from seven Canadian provinces with 1+ encounter in the Canadian Primary Care Sentinel Surveillance Network (CPCSSN) database between January 1, 2011 & December 31, 2019. The study cohort had 3 phases: Jan 1, 2011-Dec 31, 2015 (era 1), Jan 1, 2016 – Dec 31, 2017 (wash out) & Jan 1, 2018- Dec 31, 2019 (era 2). Hypertension was defined by Fourth Report up to December 31, 2017 & American Academy of Pediatrics guideline thereafter. We performed an interrupted time series analysis to assess impact of the guideline recommendations on BP screening and HTN prevalence.
Results: 264,635 children in era 1 & 193,654 children in era 2 were evaluated. In era 1 and 2, there were 66,653 (25.2%) & 45,050 (23.3%) children, respectively with at least 1 BP measurement. Annual BP screening generally increased each year from 13.3% in 2011 to 20.2% in 2019. In Era 1, a total of 1.1% of children met HTN criteria with a mean onset age of 12.6 years (SD 4.1). In Era 2, a total of 2.0% of children met HTN criteria with a mean onset age of 14.1 years (SD 4.1). Time series analysis revealed a significant increase in BP screening and HTN after the guidelines' introduction (p=0.04 and p=<.0001 respectively).
Conclusion: BP screening and HTN prevalence generally increased between 2011 and 2019, with a significant increase in post-guideline BP documentation and children meeting HTN criteria following guideline implementation.

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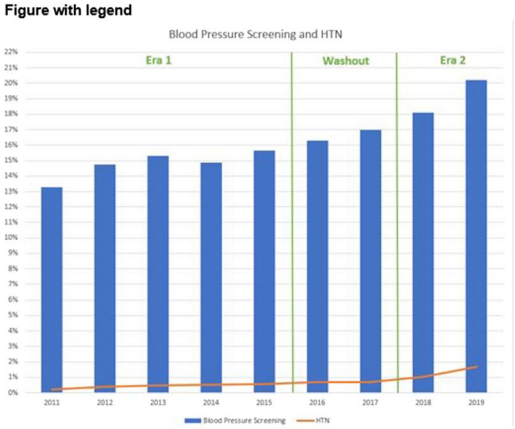

Figure 1. The proportion of children who received an annual blood pressure screening and the proportion of children who met HTN criteria from Jan 1, 2011 to Dec 31, 2019 by a primary care provider. The percentages are based on each year and as such, some children may have numerous measurements done. The NHLBI guideline was used to define thresholds for hypertension (blood pressure>95th percentile) up to Dec 31, 2017. From Jan 1, 2018, hypertension was defined by AAP 2017 guidelines as BP ≥95th percentile for age, sex and height [3-12 years] or ≥130/80mmHg [≥13 years].

Hemolytic uremic syndromes and thrombotic microangiopathy

O-23 - A new index to predict long-term renal outcome in patients with typical hemolytic uremic syndrome

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Approximately 20% of patients with typical hemolytic uremic syndrome (HUS) evolve to chronic kidney disease stage 2-5 (CKD). High leucocytes, hemoglobin (Hb), and serum creatinine (sCr) at diagnosis have been associated with worse long-term outcome, being the days of dialysis the most important predictor. Recently, Ardissino et al. reported the index Hb+2sCr as a short and long-term prognosis predictor.
Objectives: 1) to determine the best independent predictor of long-term renal outcome, 2) to evaluate a new index (Hb at diagnosis + days of dialysis).
Methods: observational and retrospective study. We included 281 patients with more than 5 years of follow-up. At last control, after a median follow-up of 12 years they were classified as Complete Recovery (CR) (n:139), CKD1 (n:104), CKD2-4 (n:27) and CKD5 (n:11). To determine predictors, variables at diagnosis (age, leukocytes, sCr, Hb), days of dialysis, Ardissino's and the new index were compared between 2 groups: favorable outcome (CR+CKD1) and CKD2-5. Bivariate and multivariate analyses were performed. Predicting progression to CKD was assessed by drawing up ROC

curves and AUC. Cut-off and OR were calculated; $p<0.01$ was considered significant.
Results: Table shows the median and means of all variables in both groups.

Table: Comparison of the median of all the variables in the 2 groups: complete recovery + CKD 1 vs. CKD 2-5

	CR + CKD 1 Median (Q1-Q3) n	CKD 2-5 Median (Q1-Q3) n	*p* value	ANOVA *p* value	n
Age (months)	19 (13;31) n=243	14.5 (9;20.25) n=38	0.035		281
Serum Creatinine (sCr) mg/dl	1.85 (1-3.38) n=164	1.8 (1.2;2.89) n=13	0.57		177
Leukocytes cel./mm^3	14900 (11575;21575) n=198	24800 (13800;33550) n=29	0.044		227
Hemoglobin * (Hb) g/dl	8.15 (1.92) n=162	9.935 (1.9190) n=20	-	0.000	182
Dialysis (days)	3 (0;10) n=243	13.5 (10;19) n=38	0.000		281
Ardissino´s index (Hb + 2 sCr)	12.57 (10.3;15.5) n=138	14.15 (12.12;15.49) n=10	0.32		148
New index (Hb + days of dialysis)	11.9 (7.7;19.2) n=162	25.15 (18.8;38.2) n=20	0.000		182
Time of follow-up (months)	149 (99;194) n=243	205 (144;247) n=38	0.001		281
Number of patients (%)	243 (86.5%)	38 (13.5%)	-		281

CR: complete recovery; CKD: chronic kidney disease; Q1: 1st quartile; Q3: 3rd quartile. * mean (standard desviation)

Age, Hb, leucocytes, days of dialysis and the new index achieved statistical significance.
Only days of dialysis and the new index were independent predictors of CKD2-5.
Comparing the AUC, the new index resulted better than Ardissino's score and days of dialysis to predict CKD2-5 (0.86; (CI 0.79-0.94), 0.53; (CI 0.37-0.69) and 0.81; (CI 0.73-0.88) respectively).
A cut-off of 18 for the new index increased 13 times the risk of CKD2-5 (CI 3.66-46.64). The optimal cut-off for the days of dialysis was 10 with an OR of 10.9 (CI 4.76-25.14).
Conclusion: The new index: Hb at diagnosis + days of dialysis resulted the best CKD2-5 predictor.

Hemolytic uremic syndromes and thrombotic microangiopathy

O-24 - Argentine cohort of 105 Hemolytic Uremic Syndrome patients followed more than 15 years. Is it enough?

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Even though most patients with typical hemolytic uremic syndrome (HUS) have a complete recovery (CR) after acute stage, chronic kidney sequelae may appear a long time later. Optimal follow-up time to early detect and treat chronic kidney disease (CKD) is unknown. Some studies reported that kidney sequelae 1 year after HUS could predict long-term prognosis.
Aims: 1) to describe long-term outcome of HUS patients according to severity of acute stage, 2) To evaluate if kidney sequelae 1 year after HUS could reflect long-term outcome.
Methods: 105 patients followed annually were retrospectively analyzed at 1,5,10 and 15 years after HUS. Kidney function after each control was categorized as CR and different CKD stages. Severity of the acute stage was evaluated based on days of dialysis, 64 patients (61%) required dialysis and 42 dialyzed >10 days.
Results: Patients in different CKD stages after 1,5,10,15 years and at last control are shown in Figure 1A. After a median follow-up of 17 years, 37% were in CKD1 and 20% in CKD2-5. Of the 41 patients with CR after 10 years, 6 (14%) progressed to CKD1-2. Figure 1B illustrates kidney function at last control according to dialysis requirement. The prevalence of CKD2-5 increased from 5% in non-dialyzed patients to 43 % in those who dialyzed >10 days.

Figure 1A: Long term outcome (n=105)

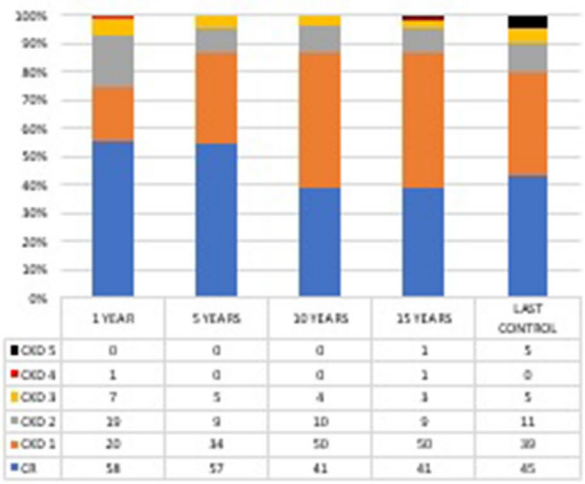
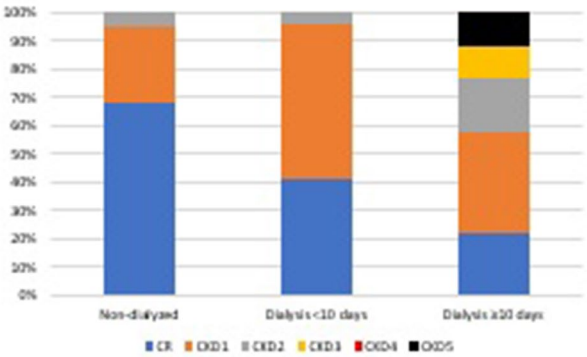


Figure 1B: Kidney function at last control according to dialysis requirement



CR: Complete recovery; CKD Crhonic kidney disease

Comparing the status 1 year after HUS with the last control, we observed that 16 (27.5%) of the 58 patients with CR after 1 year progressed to CKD1 and 6 patients (10.3%) to CKD2-5. On the other hand, 4 (14.8%) of the 27 who were in CKD2-5 in the first year achieved a CR years later.
Conclusion: Our results demonstrated that even HUS patients with CR during years need to be followed until adulthood. Kidney sequelae 1 year after HUS did not reflect long-term outcome.

Alport syndrome (and other GBM diseases)

O-25 - Pathogenicity assessment of non-glycine missense variants in COL4A5 triple-helical region

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ABSTRACT
Background: *COL4A5*, which encodes type IV collagen α5 chain, is a causative gene of X-linked Alport Syndrome (XLAS). In the glomerulus, type IV collagen α5 chain forms triple-helical structure with collagenous α3 and α4 chains. Type IV collagen α3, α4, and α5 chains consist of three domains: N-terminal domain, collagenous domain, and Non-collagenous domain. In triple-helical region of type IV collagen protein, the amino acid strictly repeats glycine (Gly) in every third position, (Gly-Xaa-Yaa)n, and these Gly contribute to the stability of triple-helical structure. Because of this, within triple-helical region, most Gly missense variants are pathogenic, and most reported missense variants substitute amino acids from Gly. However, several pathogenic missense variants other than Gly (non-Gly missense variants) have been reported and the mechanisms of disease onset by these variants are not clear until now. The aim of this current study is to investigate the pathogenicity of non-Gly missense variants in *COL4A5* collagenous domain.
Method: We extracted 19 variants, 14 from the Human Gene Mutation Database, and five identified in our cohort. Firstly, we conducted *in vitro* splicing analysis. Then, variants without aberrant splicing were investigated for their characteristics.
Result: Eight out of nineteen (42.1%) variants caused aberrant splicing. Five of the remaining 11 variants not causing aberrant splicing were missense variants substituted from Proline (Pro) located at Yaa of (Gly-Xaa-Yaa)n. Pro at this position is hydroxylated and results in the stabilization of the triple-helix structure. Two of the remaining variants were located outside of the (Gly-Xaa-Yaa)n repeat (interrupted domains). These interrupted domains are related to the flexibility of the collagen molecule. Therefore, these seven variants influence the triple-helix structure and show pathogenic.
Conclusion: We revealed the new mechanisms showing pathogenicity of non-Gly missense variants in *COL4A5* triple-helical region.

Nephrotic syndrome

O-26 - Efficacy of Levamisole for Maintaining Remission After the First Flare of Steroid Sensitive Nephrotic Syndrome in Children : the NEPHROVIR-3 randomized controlled trial

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Introduction: In children with Steroid Sensitive Nephrotic Syndrome (SSNS), relapse after the first flare occurs in 80% of cases, whatever the dosage or duration of initial steroid therapy. Therefore, there is an unmet need for early interventions to reduce incidence of early relapses. Levamisole is an antihelmintic drug with an immunomodulatory action that reduces relapses in children with Frequent Relapses or Steroid Dependant NS. NEPHROVIR-3 is the first trial to assess the efficacy of levamisole in increasing duration of initial remission after the diagnosis of INS.
Material and methods: NEPHROVIR-3 is a multicentric placebo-controlled randomized trial (1:1), in 38 centers of the Paris area, France. Patients were included at INS diagnosis and randomized, when steroid sensitive within 4 weeks, to receive either levamisole 2.5 mg/kg/48h or placebo for 6 months, in addition to the French steroid protocol (18 weeks-3990mg/m^2). Primary outcome was the relapse-free survival at 1 year. The effect of the study drug was analysed by a Cox proportional hazard model stratified on centre.
Results: Between September 2017 and February 2020, 86 patients were included, median age at INS onset was 5 yrs (IQ 3-7), with 69% of boys. At 4 weeks, 68 of them were randomized. Median time to remission was 8.5 days (IQ 6-12). Relapse-free survival at 12 months was 53.8% (95%IC 34.7-69.5) in the levamisole group versus 20.9% (7.2-39.4) in the placebo group (p=0.007). The risk of relapse associated with levamisole was HR =0.37 (95%IC 0.15-0.89). Treatment was well tolerated with one interruption in each group because of skin rash.
Conclusion: Early treatment with levamisole at the first flare of childhood SSNS is well tolerated and significantly improves relapse-free survival at 1 year.

Nephrotic syndrome

O-27 - Mycophenolate mofetil (MMF) versus cyclophosphamide (CYC) to prevent relapse in children with steroid-dependent nephrotic syndrome (SDNS): a multicentrer, randomized, controlled trial.

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Background: Previous studies demonstrated the efficacy of CYC and MMF in preventing relapses in children with SDNS but no study to date provided a clear comparison between these two treatments. This study aim at demonstrating that MMF is superior to CYC in preventing relapses in children with SDNS.
Methods: We included 70 children (2-16 years old) with SDNS from 15 centers in this open-labeled, randomized, controlled trial. Patients were included during a relapse and received a standardized steroid regimen. Oral CYC was administered at 2mg/kg/d for 12 weeks (cumulative dose 168mg/kg) and MMF at 1200mg/m²/d for 18 months.
Results: 70 children were included in 15 centers. 34 patients were randomized to receive CYC and 35 to MMF, patients' characteristics did not differ between treatment groups. There was no significant difference in relapse rates at 24 months between the CYC group (58%) and the MMF group (57%), p=0,97. There were no differences between relapsers and non-relapsers in terms of sex, disease duration and cumulative dose of steroid in the year prior to inclusion. Younger age was associated with a higher rate of relapse (75% in children <6 vs. 45% in children>6, p=0,02). Among younger children, CYC tended to be associated with a higher rate of relapse compared to MMF (86% vs. 62%, p=0,15), while no difference was found in older children. No significant differences in digestive, infectious or hematological complications were found and 4 patients (12%) in the CYC reported alopecia.
Conclusion: Overall, MMF was not superior to CYC in preventing relapse in children with SDNS. Children under 6 have the highest risk of relapse and MMF may be superior to CYC in this subpopulation.

Glomerulonephritis (including vasculitides)

O-28 - Long-term survival outcomes of children and adolescent with biopsy-proven childhood-onset lupus nephritis: a 20-year study

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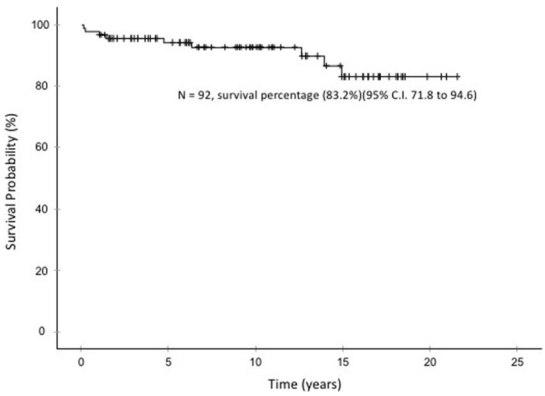
Aim: To determine the long-term outcomes in childhood-onset lupus nephritis (cLN) in a tertiary Paediatric Nephrology centre in Hong Kong.
Methods: We conducted a cohort study of biopsy-proven cLN (presenting before 19 years) between 2001-2020. Primary outcomes included patient and kidney survivals, and a composite outcome of advanced chronic kidney disease (CKD, eGFR ≤60), kidney failure and death.
Results: 92 Chinese children (Female, n=78; mean age 13.7±3.3 years) with biopsy-proven cLN were included. The mean follow-up duration was 10.3±5.9 year. 83 children (90%) had proliferative LN (Class III/IV ± V). The commonest presentation was nephritic-nephrotic syndrome (32%) and 7 patients required acute dialysis. 37 patients (40%) and 35 patients (38%) received mycophenolate and cyclophosphamide (n=35, 38%) induction respectively. The rates of complete/partial remission at 6 and 12 months were 65%/20% and 78%/8%, respectively.
Two deaths were observed over 945.9 patient-years, which conferred to a mortality rate of 2.1 deaths per 1000-patient-years (95%CI 0.3-7.6) and a standardized mortality ratio of 22.3 (95% CI 6.6 -38.1). One death was due to severe pneumonia, while the other was secondary to macrophage activation syndrome with central nervous system involvement. Three patients developed kidney failure and five had advanced CKD. The survival probabilities for the composite outcome were 96.7%, 94.2%, 92.7% and 83.2% at 1-, 5-, 10- and 15-year, respectively. Univariate analysis demonstrated that dialysis at presentation (HR 15.6, 95% CI 3.1-77.8, p<0.001), repeated relapses (6.5, 95% CI 1.3-33.6, p=0.03) and no disease remission at 12 months (HR 11.1, 95% CI 2.7-46.7, p<0.001) were associated with increased risk of reaching the composite outcome.
Conclusion: Patients with cLN show relatively favourable long-term clinical outcomes with the availability of effective immunosuppressive treatments, although they still have significantly increased mortality. Patient outcomes can be further optimized by better disease control and prevention of relapse.

Figure 1: Kaplan-Meier plot of survivals free from the composite outcome of advanced CKD (eGFR <60), kidney failure and deaths in 92 Chinese children with lupus nephritis



Glomerulonephritis (including vasculitides)

O-29 - Urinary podocyte excretion is associated with the disease severity in children with IgA nephropathy

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Background: IgA nephropathy (IgAN), as one of the most common glomerular diseases, accounted for 20% of patients which progressed to end-stage renal disease within 25 to 30 years. Urinary podocyte excretion has been reported to increase in patients with glomerular diseases. The current study aimed to determine the value of urinary podocyte excretion in children with IgAN.
Methods: IgAN and age-matched children were enrolled in this study, from Jan. 2017 to Jan. 2022. Random urine samples from IgAN were collected and stored at -80 °C. The levels of urinary podocyte excretion in the urine pellet was measured and normalized by urine creatinine (Pod/Cr).
Results: Children with IgAN (n=50) had significantly higher levels of urinary Pod/Cr compared to age-matched healthy controls

(n=23). The levels of urinary Pod/Cr were significantly positively correlated with urinary protein molecules (including 24-h urinary total protein, total protein: creatinine ratio, albumin:creatinine ratio, N-Acetyl-beta-d-Glucosaminidase:creatinine ratio, and α1-microglobulin: creatinine ratio). Patients at the stage of complete proteinuria remission had significantly lower urinary Pod/Cr than patients with proteinuria. After treatment, urinary Pod/Cr returned to normal at 6-12 months, accompanied by proteinuria remission.
Conclusions: Children with IgA nephropathy had significantly higher urine podocyte excretion than healthy controls. Urinary podocyte excretion is associated with the disease severity.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

O-30 - Long term follow-up of children with Bartter syndrome (BS). A single center experience

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Introduction: BS is a rare autosomal recessive renal tubular disorder. Little information is available on the long term outcome of these patients.
Methods: Clinical and laboratory data of patients with BS at diagnosis and long term follow up (2-21, median 10 years) are reported in 18 children: 16 Caucasian and 2 of gipsy origin.
Results Genetic testing was done in 13/18 patients (11males, 7 females) and revealed 6 mutations in KCNJ1 genes, 5 in SLC12A1 and 2 in CLCKNB genes. 4 new mutations were identified (3 in KCNJ1 genes and 1 in SLC12A1). All children were born pre-term. 4/6 patients with KCNJ1 mutations presented initially with hyperkalemia. 16/18 patients (included the 2 patients with CLCKNB mutations) had nephrocalcinosis grade I-III, 1 with KCNJ1 mutation nephrocalcinosis grade IV. 17/18 patients had hypercalciuria. Medical treatment in the last follow up included supplementation with potassium (0.33-1.5 mmol/kg/day) in 18, indomethacin (0.25-2.3 mg/kg/day, median 0.9mg/kg/day) in 15 and gastroprotective drugs in 13. At last follow up, body weight and height were within normal ranges in 13/18 patients (4/5 patients with height<3rd percentile were not compliant with treatment). All had normal neurodevelopmental outcome. Two patients received recombinant growth hormone due to growth hormone deficiency. Glomerular filtration rate was <90 ml/min/1.73m^2 in 5/18 (2 had chronic kidney disease stage 3 and 3 stage 2). Of note, 2/5 had impaired renal function since diagnosis (1 with SLC12A1 mutation and 1 with KCNJ1) while the remaining 3/5 (2 with KCNJ1 and 1 with SLC12A1) progressed gradually during follow up .
Conclusions: Patients with BS tend to present a satisfactory prognosis. The findings of this study emphasize the need for early diagnosis, regular follow up, evaluation of renal function and appropriate treatment in order to maintain normal renal function and achieve normal final height and weight.

Transplantation (including CMV, EBV & BK infections)

O-31 - Multicentre study of incidence, risk factors, treatment and outcome of antibody-mediated rejection in paediatric kidney transplant recipients – an analysis of the Cooperative European Paediatric Renal Transplant Initiative CERTAIN

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Introduction: Late antibody-mediated rejections (ABMR) are one major cause for premature kidney transplant (KTx) loss in adults. However, data on incidence, risk factors, treatment strategies and outcome of ABMR in paediatric patients are scarce. Therefore, the aim of this work was to investigate this topic within the framework of the paediatric European Transplantation Research Network CERTAIN.
Methods: Data on donor-specific HLA antibodies (HLA-DSA), biopsy findings, immunosuppressive therapy and graft function were documented in specific query forms in CERTAIN. Inclusion criteria were (i) regular monitoring of HLA-DSA (by SAB-assay) at least once per year posttransplant and/or (ii) at least one HLA-DSA measurement at time of a clinically indicated KTx biopsy.
Results: 19 centres from seven European countries participated in this study. Until September 2021, 331 patients, who fulfilled the inclusion criteria, were documented. The cumulative incidence of acute ABMR up to 5 years posttransplant was 10.8%, and that of chronic ABMR was 5.9%. Risk factors for the development of ABMR were the number of HLA-mismatches, evidence of *de novo* DSA, and T-cell-mediated rejection (TCMR) before ABMR. ATG or monoclonal antibodies were used in 65% of ABMR episodes; IVIG were applied in 48%. 81% of patients received a tacrolimus-based maintenance immunosuppression. By multivariate analysis, ABMR (HR 2.9; p<0.001), TCMR (HR 2.1; p=0. 02), and BK polyomavirus-associated nephropathy (HR 4.2; p<0.001) were relevant risk factors for premature graft function deterioration, defined as eGFR <50% of baseline or eGFR <30 mL/min*1.73 m^2 BSA).
Discussion: The results underscore the importance of ABMR as major risk factor for premature graft function deterioration in paediatric KTx recipients. There was considerable variability among centres regarding treatment of ABMR subtypes. Standardization of treatment of ABMR by an evidence-based guideline and the introduction of novel drugs for more effective therapy are urgently needed to improve outcome.

Transplantation (including CMV, EBV & BK infections)

O-32 - Landscape of subclinical rejection in a large international cohort of pediatric kidney transplant (kTx) recipients

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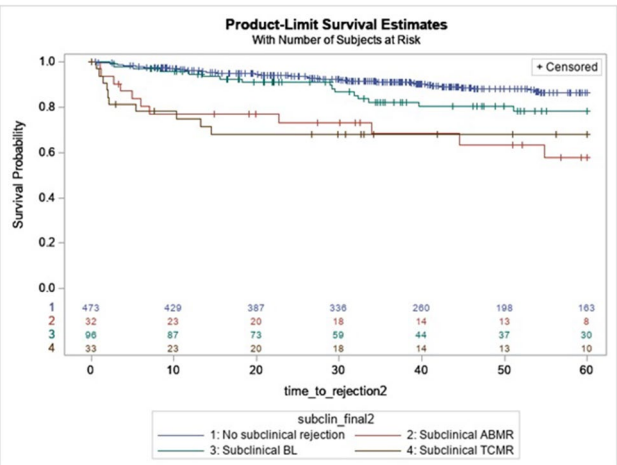
Background: Kidney allograft rejection can occur in clinically stable patients, but long-term significance in pediatric kTx recipients is unknown. Previous single-center studies demonstrated that subclinical borderline (SC-Borderline) or T-cell mediated rejection (SC-TCMR) are associated with an increased risk of acute rejection. However, the prevalence and significance of subclinical antibody-mediated rejection (SC-AMR) and the impact of subclinical rejection phenotypes on graft survival remained to be assessed.
Methods: We used data from pediatric (<21) patients transplanted between 2005 and 2017 from 8 institutions in France and the United States performing surveillance biopsies. Biopsies were identified as surveillance if they were recorded as such in the medical record with no significant increase in serum creatinine or proteinuria. Biopsies were graded according to the Banff 2019 criteria. DSA screening was performed according to each center protocol. Kaplan Meier method and log-rank test were used to compare the risk of acute rejection, transplant glomerulopathy and graft loss stratified on the surveillance biopsies' findings.
Results: 1390 surveillance biopsies were performed in 763 kTx recipients including 135 (9,7%) SC-borderline, 46 (3,3%) SC-TCMR, 54 (3,9%) SC-ABMR, 8 (0,6%) subclinical mixte rejections. Subclinical rejection was associated with acute rejection with 5-year rejection-free survival of 88%, 78%, 68% and 63% in the no rejection, SC-borderline, SC-TCMR and SC-AMR groups, respectively (p<0,0001). SC-TCMR and SC-AMR were associated with the development of transplant glomerulopathy, p<0,0001. Subclinical AMR only was associated with a lower 5-year graft survival (79% vs. 93% (SC-TCMR), 95% (SC-Borderline), 94% (no rejection)), p=0,002.
Conclusion: Subclinical rejection is prevalent in pediatric kidney recipients without clinical dysfunction and is associated with acute rejection. Subclinical AMR is associated with the development of transplant glomerulopathy and with an increased risk of allograft failure.



Transplantation (including CMV, EBV & BK infections)

O-33 - Exploring patient, family and clinician perspectives about the psychosocial factors influencing access to kidney transplantation and transplant outcomes for children

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Introduction: Kidney transplantation is often seen as the optimal form of kidney replacement therapy for children and young people (CYP) with stage 5 Chronic Kidney Disease (CKD5). Psychosocial factors have been cited to delay their access to a kidney transplant, however it is unclear what these factors are.
We undertook a multi-centre qualitative study that explored the range of psychological and social factors that CYP, their carers and their paediatric nephrology multi-disciplinary team (MDT) perceived to influence how soon a CYP with CKD5 accesses a kidney transplant. This included factors that were perceived to influence kidney transplantation outcomes or deemed important to patients and their families in terms of their quality of life (QoL).
Material and methods: Semi-structured interviews were conducted with CYP, their carers and their paediatric nephrology MDT across 7 tertiary paediatric nephrology units in the United Kingdom. These interviews were reviewed for pertinent themes using thematic Analysis following the approach of Braun and Clarke.
Results: A total of 36 interviews were conducted with 13 families and 16 members of the paediatric nephrology MDT. The majority of participating families identified as White (57%), followed by Black (22%) or Asian (21%). The following themes were deemed important to accessing kidney transplantation and post-transplant outcomes: health beliefs; relationship with and trust in healthcare; support networks; family relationships; socioeconomic circumstances; culture and race; and mental health and coping strategies. Specific challenges from living with CKD5 and living through the COVID-19 pandemic were also discussed due to their impact on QoL and accessing a kidney transplant.
Conclusions: There are a wide range of psychosocial factors that are perceived to influence a CYP's access to kidney transplantation. Longitudinal and prospective studies are needed to fully assess the relationship between these psychosocial factors and a CYP's access to, and outcomes of, kidney transplantation.

Transplantation (including CMV, EBV & BK infections)
O-34 - Application of HLA molecular mismatch algorithms to predict primary alloimmunity risk and rejection in paediatric kidney transplantation

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Introduction: Immune recognition of donor HLA mismatches and subsequent graft rejection remains a major cause of graft deterioration in paediatric kidney transplantation. We aimed to assess the potential of computational methods of assessing HLA immunogenicity (molecular mismatching, molMM) and of classical antigen mismatching (antMM) to predict primary alloimmunity risk.
Methods: We performed a retrospective analysis of 177 paediatric patients (median age 10.8 [IQR] 5-15 years) from the ABMR study from the CERTAIN registry, all of whom had prospective monitoring of donor-specific antibody (DSA) post-transplant. We compared four molMM methods: amino acid mismatch scores (AAMS, assessing T- and B-cell alloimmunity), electrostatic mismatch score-3-dimensional (EMS3D, B-cell alloimmunity), and NetMHCIIpan (T-cell alloimmunity) at HLA-peptide affinity binding thresholds of 500nM (netMHC) and 1000nM (netMHC1k as implemented in the PIRCHE algorithm).
Results: *De novo* DSA incidence was highest against HLA-DQ (30/177, 17%, Table1). Higher antMM and molMM were associated with DSA formation. DSA preferentially targeted the highest scoring molMM allele in each individual patient. MolMM methods were more predictive of DSA compared to antMM (Table1, AUROC results), and EMS3D was the most consistent predictor across all HLA loci (AUROC 0.72-0.75). Biopsy proven ABMR (11/177, 6%) was associated with increasing recipient age and Class II molMM (defined by AAMS or EMS3D or netMHC). Late TCMR (>6 months) was diagnosed on for-cause biopsies in 23 (13%) patients. Accounting for the total HLA burden, neither molMM nor antMM scores were predictive of TCMR outcome.
Summary: Molecular HLA mismatching enabled better prediction of primary alloimmunity risk compared to conventional antigen mismatching. Incompatibility at the HLA-DQAB loci was the main driver for TCMR and ABMR.

HLA loci (number of DSA, %)	A (22, 12%)	B (15, 8%)	DQ (30, 17%)	DR (25, 14%)
Antigen	0.63	0.46	0.56	0.57
AAMS	0.71	0.67	0.72	0.74
EMS3D	0.74	0.72	0.75	0.73
netMHC	0.71	0.57	0.64	0.69
netMHC1k	0.73	0.52	0.76	0.70

Table1: Area under the receiver operating characteristic curve (AUROC) results for each molMM method compared with antMM. Analysis was performed using the highest score of both alleles, using logistic regression for each HLA allele separately.

Urology (including UTIs, kidney stones and bladder dysfunction)

O-35 - Desmopressin plus tolterodine versus desmopressin plus indomethacin for pediatric enuresis: An open-label randomized clinical trial

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Background: Nocturnal enuresis (NE), defined as bed wetting with urine in children aged >5 years for at least 3 consecutive months, is of clinical significance. In the current study we aimed to compare the effects of desmopressin plus tolterodine with desmopressin plus indomethacin for the treatment of pediatric enuresis.
Methods: This open-label randomized clinical trial included 40 children aged >5 years diagnosed with monosymptomatic (only NE) and disymptomatic (NE plus diurnal enuresis) primary enuresis referred to the Nephrology Clinic of Bandar Abbas Children's Hospital, Hormozgan, Iran from March 21, 2018 to March 21, 2019. Age, gender, family history of enuresis, history of consistent incontinence from the age of toilet training, and concurrent diurnal enuresis were recorded. Patients were randomized into two groups (n=20). Children in the desmopressin + tolterodine group [D+T] received 60 µg sublingual desmopressin and a 2 mg tolterodine tablet, while children in the desmopressin + indomethacin [D+I] group received 60 µg sublingual desmopressin and two 25 mg (50 mg) indomethacin capsules every night before bedtime for 5 months. Reduction in the frequency of enuresis and response to treatment were evaluated at 1, 3, and 5 months. Drug reactions and complications were also noted.
Results: The two study groups were comparable regarding age, gender, family history of enuresis, history of consistent incontinence from the age of toilet training, and concurrent diurnal enuresis. Reduction in the frequency of enuresis was significantly higher in the D+T group compared to the D+I group at all time points. Complete response to treatment at the end of the study period was significantly higher in the D+T group (50% vs. 0%, P=0.001). No drug reactions of complications were observed in any of the groups.
Conclusions: Desmopressin plus tolterodine appears to be superior to desmopressin plus indomethacin for the treatment of pediatric enuresis refractory to desmopressin.

Urology (including UTIs, kidney stones and bladder dysfunction)

O-36 - Efficacy and tolerance of Stiripentol in patients with primary hyperoxaluria (PH)

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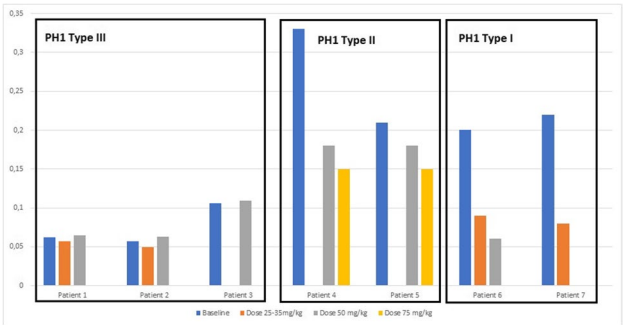
Background: Stiripentol, an approved antiseizure drug, was shown to decrease in a dose-dependent manner the synthesis of oxalate by hepatocytes *in vitro* and to significantly reduce urine oxalate excretion *in vivo* after oral administration.
Methods: We reviewed the efficacy and tolerance of Stiripentol in patients treated for PH in our center within an open-label, prospective trial or for compassionate use. Stiripentol was initiated at 30mk/kg/day in patients over 12 years and 50mg/kg/day in younger patients and increased to 50mg/kg/day (>12) or 75mg/kg/day (<12) if well tolerated. Efficacy was assessed based on uOx/creat ratio in mmol/mmol (median of 3 consecutive measures for each time point).
Results: 7 patients were included, 2 patients with PH1 type II and 3 patients with PH1 type III were included within the clinical trial and 2 PH1 type 1 were included after screening failure for iRNA trials (reason for failure were low eGFR in one and uOx/creat ratio below threshold in the other). Age at treatment initiation ranged from 2 to 19 year old. Figure 1 displays the evolution of uOx/creat under treatment. Median change uOx/creat ratio was +4.8% in type III, -41% in type II and -67% in type I, respectively. In one type I patient (patient 7), stiripentol was initiated under stable regimen of pyridoxine and Lumasiran. Overall, the treatment was well tolerated and treatment

duration ranged from 3 months (duration of the trial) to 36 months and only one patient discontinued the treatment because of abdominal pain and loss of appetite.
Conclusion: We observed a decrease in urinary oxalate excretion in patients with PH1 type I and II. Stiripentol may be effective in reducing oxalate excretion either alone or in association with iRNA treatment in patients with insufficient response. No change in oxalate excretion was found in type III with low baseline ratio.

Figure 1



Urology (including UTIs, kidney stones and bladder dysfunction)

O-37 - Histone deacetylase inhibitor therapy boosts RNase 4 and 7 expression and protects against invasive uropathogenic E. coli infection.

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Urinary tract infection (UTI) is one of the most common infections encountered in medicine. Girls and women who experience a UTI are at increased risk for recurrent UTI, especially with multidrug resistant (MDR) bacteria. Recurrent UTI may result in kidney injury and scarring. Thus, it is critical to identify antibiotic-sparing therapies to treat UTI and overcome the challenges associated with MDR-pathogens. Antimicrobial peptides (AMPs) are attractive candidates for new UTI therapies because they have potent antibacterial activity, low bacterial resistance, and exhibit synergy with antibiotics. In the urinary tract, Ribonuclease (RNase) 4 and 7 are AMPs secreted by kidney collecting duct and bladder urothelial cells and efficiently kill uropathogenic *E. coli* (UPEC) and MDR-UPEC. The goal of this project was to identify commonly used medications that can enhance RNase 4 and 7 expression. We generated reporter kidney cells expressing firefly luciferase under the control of human *RNASE4* or *RNASE7* promoters. Next, we subjected these reporter cells a library containing 1,280 FDA-approved drugs. This high-throughput screen identified histone deacetylase inhibitors (HDACi) as the most common medications that induce RNase 4 and 7. We validated HDACi-mediated induction of endogenous RNase 4 and 7 in primary human bladder and kidney cells via qRT-PCR, Western blotting, and ELISA. We identified the class I HDACi, MS275 (entinostat), as a selective and potent AMP inducer. To confirm these findings *in vivo*, we treated mice with intraperitoneal MS275. Western blot showed that MS275 treatment enhanced urothelial AMP expression. When mice were subjected to experimental UTI, MS275-treated mice had 4-fold less UPEC in their urine compared to vehicle-treated mice. These findings show that HDACi boost RNase 4 and 7 expression and reduce UTI susceptibility. Identification of strategies to enhance host AMP expression represents a paradigm shift away from conventionally used antibiotics as UTI therapies.

Miscellaneous (topic not included elsewhere)

O-38 - Neonatal kidney stem/progenitor cells injection induce SIX2 reactivation in donor human kidneys

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Background: The unique SIX2+ stem cell population gives rise to the formation of all nephron structures in the developing kidney and is exhausted before the 36th week of gestation, when after, no new nephrons are formed. We have previously described a unique non-invasive strategy to isolate and expand the native SIX2+ kidney stem cells from the urine of preterm neonates, named neonatal kidney stem/progenitor cells (nKSPC).
Methods: We analysed the mechanism of immunosuppression of nKSPC using mixed lymphocyte reactions and HPLC-MS. Then, we administered nKSPC into human kidneys discarded for transplantation during 6h of normothermic machine perfusion. We analysed the immunomodulatory and regenerative potential of nKSPC therapy by differential gene and protein expression in the tissue and perfusate solution.
Results: nKSPC administration in donor kidneys had an immunosuppressive potential, by reducing inflammatory cytokine levels via the tryptophan-IDO-kynurenine pathway, and significantly lowering the levels of kidney injury biomarkers. We could track nKSPC in the kidney tissue and most impressively, we showed that nKSPC treatment induces the *de novo* expression of SIX2 in proliferating proximal tubular cells, which suggests the induction of an endogenous regenerative process. This is the first time that the latter phenomenon has been reported.
Conclusions: nKSPC might be the ideal cell type to be applied in kidney-targeted cell therapy, providing immunomodulation and inducing an endogenous regenerative process.

POSTERS

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-001 - A retrospective study to assess the clinical utility of voiding cystourethrogram after a first renal abscess in otherwise healthy children

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Background: Approximately 25-30% children with a first urinary tract infection (UTI) have vesicoureteral reflux (VUR), as assessed by the voiding cystourethrogram (VCUG). The indications for this expensive and invasive procedure have been greatly reduced in the past years. They are now restricted following the second UTI or following the first UTI in cases with abnormal ultrasound, and/or high fever with non-E.Coli pathogen and/or renal scarring. We ought to assess the clinical utility of this test after a first renal abscess in otherwise healthy children.
Material and methods: A retrospective single-center case review was conducted in healthy children diagnosed with a first renal abscess between 2011-2022. Eighty-seven children with a history of uropathy or UTI, septicemia, or immunosuppression were excluded.
Results: The 17 included children, aged 1 months-14 years, underwent ultrasound examination and VCUG. VUR was identified in 5/17 (29%) cases, 2/17 (12%) with grade IV-V. Ultrasound and VCUG findings were not correlated.
6/16 identified pathogens were non-E.Coli pathogens (proteus, klebsiella, enterococcus, staphylococcus);1/6 non-E.Coli abscess was associated with VUR.
The treatment consisted of i.v. antibiotics (10-21 days Cephalosporins+5 days aminoglycosides), then oral treatment for 2-6 weeks. One received 6-month-trimethoprim-sulfamethoxazole antibiotic prophylaxis.
Nine (53%) children had a favorable outcome. 8/17 had renal scars, 3/8 developed kidney hypotrophy. None had chronic kidney disease. 5/17 had recurrent UTIs, of whom 4 underwent surgical treatment (1 posthectomy, 1 endoscopic Deflux injection, 1 ureteral reimplantation, 1 nephrectomy for renal non-function). Three with VUR but no UTI recurrence were not operated (2/3 had scars).
Conclusions: The incidence of VUR after a 1st renal abscess or after a 1st uncomplicated UTI, was similar. Surgery was indicated following UTI recurrence but not based on the degree of VUR. These results suggest that the same indications of VCUG should be used whether after a first episode of simple UTI, or after a first renal abscess.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-003 - Iroquois homeobox factors control murine nephron number

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Low nephron number is a leading cause of end stage kidney disease in children and an antecedent cause of adult-onset cardiovascular disease. Yet, molecular mechanisms that control nephron number are largely undefined. The Iroquois (*Irx*) family of transcription factors play critical roles in tissue patterning and specification in nonrenal tissues. Six *Irx* genes exist in mice, organized into clusters A (*Irx1/2/4*), and B (*Irx3/5/6*). Limited analysis of mice with *Irx3/5* deficiency suggests a decrease in nephrogenic structures.
We hypothesize that *Irx* genes control nephron number during murine renal development.
Irx genes were deleted in the *Six2+* nephrogenic lineage in a Cre-dependent manner. Nephrons were quantified by analysis of kidney tissue sections stained with the Periodic-Acid Schiff (PAS) agent. Statistical significance was assessed using Students t-test (two-tailed). Analysis of mice with germline deletion of *Irx1* ($Irx1^{tm1}$) at E18.5 demonstrated a significant decrease in kidney weight: body weight (KW/BW) ($p < 0.001$; $n = 3$) and a decrease in nephron number ($p = 0.36$; $n = 3$). To determine the direct role of *Irx1* in nephrogenic progenitor cells, *Irx1* was deleted in *Six2+* cells in a Cre-dependent manner. Analysis of E18.5 *Six2-Cre;* $Irx1^{loxP/-}$ kidneys demonstrated a 25% reduction in KW/BW ($p < 0.0001$; $n = 4$), and a 34% reduction in nephron number ($p < 0.01$; $n = 4$). To determine the functional contribution of *Irx3/5*, analysis of E18.5 *Six2-Cre;* $Irx3/5^{loxP/loxP}$ kidneys demonstrated a 34% reduction in KW/BW ($p < 0.0001$; $n = 4$), and a remarkable, 59% reduction in nephron number ($p < 0.0001$; $n = 4$). Together, these results demonstrate that genetic deletion of either *Irx3* and *Irx5* or *Irx1* in mouse nephrogenic progenitor cells causes renal hypoplasia and nephron deficiency. Our data provide a foundation to investigate molecular mechanisms by which *Irx* genes function during nephrogenesis.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-004 - Retrospective Analysis Of Congenital Abnormalities Of Kidney And Urinary Tract (CAKUT) In Children In Tertiary Care Centre Of a Developing Country.

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ABSTRACT
Background and objectives: Congenital anomalies of kidney and urinary tract(CAKUT) are abnormalities affecting-the kidneys and other structures of the urinary-tract. This study was-aimed to find the incidence of CAKUT along-with other-associated-anomalies.
Methods: 2 year Retrospective-study, was conducted during the period-of January 2020 to December 2021 in department of-Paediatrics, KLES Dr.Prabhakar-Kore-Hospital and Medical-Research-Centre,-Belagavi. The diagnosed-CAKUT cases were-included in the-study and-evaluated for-CAKUT and-other-associated-anomalies. Old known cases of CAKUT-were excluded from the study
Results: During-this two-year study period there was 18,272-registrations in the paediatric OPD and ward. Among them-104 cases were-diagnosed to have-CAKUT. Most commonest presentation was UTI. Hence, the-incidence of CAKUT was 0.28% or 2.8 per 1000 children-per year. Hydronephrosis secondary-to-pelvi-ureteric junction-obstruction-PUJO-(23.07%) was-the commonest CAKUT anomaly followed by-vesico-ureteric-reflux(20.19%). Of the associated-anomalies,13.46% of-the children-with anorectal-malformation was the common associated-malformation-noted. Majority of study-subjects were males(84.61%) and most of the children-belonged to the group<1 year(47.11%). Most of the-children with-hydronephrosis due to PUJO-belonged to the group<1 year (60%). Surgery was done in 33% of patients primarily for CAKUT. Gestational-diabetes-mellitus and pregnancy-induced-hypertension were the common-risk factors noted in 8.7% each.

Conclusion and Interpretation: Incidence of CAKUT in children aged from one month to 18 years is 2.8 per 1000 children. Hydronephrosis and vesicoureteric reflux are the most common anomalies. Early recognition of CAKUT, their treatment and close followup of these children is required for better outcome.
Keywords: Congenital anomalies of kidney and urinary tract; CAKUT; Hydronephrosis; vesicoureteric reflux.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-005 - Exosomes secreted by human urine-derived stem cells ameliorate the defects in common nephric duct remodeling and vesicoureteral reflux in Robo2-mutant mice

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Disruption of ROBO2 in humans causes congenital anomalies of the kidney and urinary tract (CAKUT). Our previous study verified that nondilating vesicoureteral reflux (VUR) is the most common abnormality in *Robo2*-mutant mice. VUR and other CAKUT malformation is the leading cause of end stage of renal disease in Children. Exosomes secreted by human urine-derived stem cells (hUSCs-Exo) have the potential to prevent kidney injury in animal models. Whether hUSCs-Exo can influence the occurrence or development of VUR/CAKUT remains unclear.
Here, we tested the real-time expression of Robo2 in whole embryos and kidney rudiments at different embryonic days to verify that there was Robo2 expression during the early nephrogenesis period. Moreover, we observed the ureteric bud (UB) outgrowth and branching, and common nephric duct (CND) remodeling in Robo2 mutant mice to validate that disruption of Robo2 causes VUR via impacting UB outgrowth and CND remodeling. Finally, we tried to apply hUSCs-Exo in vivo and in vitro to rescue the CND anomalies in the Robo2 mutant kidney rudiments, we discovered that hUSCs-Exo which enriched with the GDNF pathway signal moleculars, including ROBO2,GDNF, and RET, could be able to transmit from maternal vein to ureteral buds of fetus in mice, and rescue the CND remodeling failure and VUR in Robo2 mutant offspring .
Taken together, this study indicates that hUSC-Exo can be used as a novel promising strategy for VUR/CAKUT, which highlights the application of hUSC-Exo.
Keywords: Exosomes secreted by human urine-derived stem cells; Robo2; Common nephric duct; vesicoureteral reflux (VUR); Congenital anomalies of the kidney and urinary tract (CAKUT).

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-006 - Non organic bladder dysfunction in urinary tract infection

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Introduction: Bladder dysfunction may be due to an organic or functional cause. We can detected in imaging studies or with anamnesis and urodynamic study (UD).
Objetive: To determine the usefulness of the UD in patients with urinary tract infection (UTI) and the incidence of scar and vesicoureteral reflux (VUR) in patients with functional bladder dysfunction.
Material and Methods: Retrospective descriptive study. We review UD performed between January 1, 2019, and December 31, 2020. Inclusion criteria: patients with functional bladder dysfunction detected by the presence of UTI. Exclusion criteria: organic cause.
Results: Thirty-four patients who underwent UD were included. Women 67%; Men 33%. The median age of onset of symptoms was 5 years and 9 months. The symptoms presented were daytime incontinence 64%, nocturnal incontinence 53% and encopresis 14%. The alterations of the urinary tract that were found prior to the study: VUR in 41% and renal scars in 44%. Chronic kidney disease was presented in 11% of patients at diagnosis and it was developed in 5% in evolution. The diagnosis of the UD was the presence of uninhibited contractions 26.2% and bladder-sphincter incoordination 8%, although it was normal in 47%. The presence of associated symptoms was not related to the pathological study. The following treatments were performed: anticholinergics 67% at some point during their follow-up, biofeedback 44%, botulinum toxin 2.9%, and clean intermittent catheterization 17.6%. Psychological cares were received in 12%. The evolution of the symptoms of these patients were the resolution in 67%.
Conclusions: The urodynamic study showed functional alterations in a high percentage of patients with UTI. Daytime or nocturnal enuresis did not correlate with a greater presence of pathological studies, which makes it difficult to establish the indication based on symptoms. Patients with UTI with functional bladder disorder have a high incidence of VUR and renal scarring.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-007 - Bicentric clinical spectrum of congenital anomalies of the kidney and urinary tract in Haitian children

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Background: Congenital anomalies of the kidney and urinary tract (CAKUT) are common in children and are characterized by structural and functional abnormalities of kidney, collecting system, bladder and urethra. The malformations can be unilaterally or bilaterally sided; also they may occur in syndromic forms with other organ defects. CAKUT are responsible for 40-50% of end-stage kidney disease in children worldwide. In Haiti the leading causes of chronic kidney diseases in children are glomerular diseases.
Methods: We reviewed the medical records of all children of 0-17 years followed at the weekly pediatric nephrology clinic from January 2017 to December 2021 in Hospital St Damien Nos Petits Freres et Soeurs and in Pediatrics unit of Hopital de l'Universite d'Etat d'Haiti. Fifty-six patients with a diagnosis of CAKUT were enrolled and evaluated clinically with antenatal findings, serum biochemistry and ultrasound of urinary tract. The other imaging scans were not done due to their high cost.
Results: The male to female sex-ratio was 4.6 and the mean age was 6.1 years (0.6-17.8). The most common anomaly was posterior urethral valves (26, 46.4%), unilateral hydronephrosis (14, 25%), pelviureteral

junction obstruction (3, 5.4%) and VACTERL syndrome (3, 5.4%). Most of the anomalies have been identified postnatally during an episode of urinary tract infection or for voiding disorders.
Conclusion: The clinical pattern of CAKUT in the cohort is variable and the severity of the underlying anomalies is a crucial parameter for the prognosis. Timely detection and optimal management of the CAKUT is essential for improving the kidney health of the patients. We need to continue the advocacy for better kidney care for all the children in the countries with CAKUT by emphasizing better education of the healthcare workers and minimizing the out-of-pocket expenses for the Haitian families.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-008 - The ClinGen CAKUT Gene Curation Expert Panel

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Congenital anomalies of the kidney and urinary tract (CAKUT) constitute 20-30% of all anomalies in the prenatal period, with the spectrum of presentations ranging from mild, asymptomatic malformations, to severe, life-threatening pathologies. To date, more than 200 genes have been asserted in the literature to be associated with CAKUT however, the clinical validity of many of these associations is yet to be confirmed. Genomic medicine holds enormous promise for transforming the diagnosis, care, and treatment of patients and their families, but to reach its full potential, systematic evaluation of the validity of gene-disease associations (GDAs) and accurate assessments of variant pathogenicity are required.
The ClinGen CAKUT Gene Curation Expert Panel (CAKUT GCEP) was approved in April 2022 and will use ClinGen's established framework to classify the clinical validity of GDAs for both isolated and syndromic forms of CAKUT. The initial focus, however, is on Mendelian disorders arising from disease-causing variants in the genes most frequently implicated in CAKUT, as well as those with conflicting interpretations of significance - comprising a list of 75 genes. GDAs are curated according to the current ClinGen SOP, in conjunction with additional guidance developed by ClinGen's Kidney Disease CDWG to promote consistency between curations and evidence interpretation across the spectrum of nephropathies. The GCEP is also contributing to ongoing efforts to establish consensus recommendations for disease ontology. At present, the GCEP includes 6 curators and 12 experts with a broad range of experience from 13 organizations across 4 continents, including academic institutions, hospitals, and clinical laboratories.
The work of the CAKUT GCEP will address a critical gap in gene curation efforts and provide a way to efficiently define the clinical relevance of genes and variants across the spectrum of CAKUT, helping to ensure diagnostic accuracy as genomic testing moves to be commonplace in nephrology clinics.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-010 - Screening of vesicouretal reflux with contrast-enhanced voiding urosonography in children

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Abstract Objective: To investigate the clinical value of contrast-enhanced voiding urosonography(CeVUS) in children with vesicoureteral reflux. Methods: Children admitted to Wuhan Children's Hospital who met the CeVUS examination indications were collected, and CeVUS examination results were retrospectively analysis. RESULTS: 215 children underwent CeVUS examination, including 102 males and 113 females, aged from 1 to 115 months. ① There were 163 children with urinary tract infection (with or without fever) for the first time giving CeVUS examination,median age 6 months, 95%CI[1-98],77 were males (154PUUs) with 35 VURs (45.5%), 86 were females (172 PUUs) with 39 VURs (45.3%). For 123 cases (75.5%) from 0 to 12 months, 59 cases (47.9%) were VUR; 17 cases (10.4%) from 13 to 24 months, 8 cases (47.1%) were VUR;23 cases (14.1%) were older than 25 months, 7 cases (30.4%) were VUR. ② Results of VUR follow-up by CeVUS, there were 22 patients (44 PUUs), 14males (28PUUs) and 8 females (16 PUUs), which diagnosed with VUR by VCUG. All the 44PUUs, 9PUUs were low-grade VUR, 27PUUs were middle-high grade VUR.The follow-up examination of CEVUS showed that there were still 25 cases with reflux (56.8%). During the follow-up and compared with the VCUG,4 cases of VUR disappeared,10cases (45.5%) were improved, 5 cases (22.7%) maintained, and 3 cases (13.6%) deteriorated.The 9 children with VUR were confirmed by CeVUS for the first time, and followed up by CeVUS again. There were 7 males (14 PUUs) and 2 females (4 PUUs), and the average follow-up time was 12.7 months. One case was improved, 6 cases were maintained, and 2 cases were deteriorated. ③ There were no contrast media-related adverse events by CeVUS. Conclusion: CeVUS can be used in screening and follow-up of VUR, and is safe and feasible.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-012 - Clinical-Genetic Associations in Patients with Congenital and Infantile Nephrotic syndrome

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Introduction: Congenital nephrotic syndrome (CNS) affects the slit diaphragm in glomerular basement membrane of podocytes. The disease manifestation appears within the first three months of life in CNS and between 3-12 months for infantile nephrotic syndrome (INS) and include nephrotic-range proteinuria, hypoalbuminemia and edema. The most common cause of CNS and INS is mutations in the NPHS1 and NPHS2 genes encoding nephrin and podocin respectively. The study aimed to establish specific genetic characteristics of CNS and INS in the North American population and reveal genetic-clinical associations.
Methods: Eleven Pediatric Nephrology Consortium (PNRC) sites collected patient data retrospectively by chart review. Total 36 patients born between 1998 and 2019 and underwent genetic evaluations were included in the study.
Results: *NPHS1* mutations were more often seen in CNS patients (27/36; 75%), whereas the INS group had more frequent mutations of *WT1* (3/11;27.2%) and *NPHS2* (4/11;36.3%) genes. Among patients with *NPHS1* mutations, the splice site had a greater number of mutations than the coding region of the gene, irrespectively of the group. Among these mutations, IVS17-1 G>A splice mutation was found in 4 subjects that showed aggressive features of CNS. Interestingly, pathogenicity of the mutation confirmed by ClinVar, SNP, Human mutation database.
In patients with CNS, the frequency (9/18;50%) of multiple mutations of the *NPHS1* gene was higher than in the INS group (2/5;40%) and significantly associated with hyperproteinuria (p=0.021) and hypoalbuminemia (p=0.03). Albumin infusions were much more effective in CNS patients who had *NPHS2/WT1* mutations than those with *NPHS1* mutations. In INS patients with *WT1* mutations albumin infusions were less effective in supporting serum albumin levels
Conclusion: Variations in splice sites, specially IVS17-1 G>A and the presence of multiple mutations in *the NPHS1* gene appear to greatly impact the severity of the clinical course among patients with both CNS and INS.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-013 - Being aware of diverse renal manifestations in children with Alagille syndrome is essential

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Alagille syndrome(ALGS) is a liver disease involving cardiac, skeletal, ocular, and facial features. Renal involvements are documented in 40% of pediatric ALGS. The most common feature reported is renal dysplasia, followed by renal tubular acidosis(RTA). This study aimed to represent the prevalence, clinical manifestations, and outcomes of renal involvement in ALGS.
A total of 21 ALGS patients, under 18-year-old, who visited Samsung Medical Center from Mar, 1999 to Mar, 2022 were enrolled. ALGS was diagnosed either by clinical manifestations, targeted JAG1 sequencing, and/or liver biopsy. Medical records including sex, age, renal manifestations, urinalysis, serum creatinine, and ultrasonography were retrospectively reviewed.
The male-to-female ratio was 3:4 and ALGS were diagnosed at age between 0.3 to 46.2months. Of all, 16 patients have done targeted sequencing and 15 were detected JAG1 mutations. Renal involvements were found in 10(48%) patients, 6/15(40%) from JAG1-mutated group and 4/6(67%) from the other. Renal dysplasia defined as cystic lesions was the most common feature, shown in 3 individuals. One of them was confirmed glomerular lipid deposition pathologically. Nephrocalcinosis(NC)/nephrolithiasis(NL), vesicoureteral reflux(VUR)/pelviectasia and RTA were found in 2 individuals respectively, while one showed proteinuria. Excluding 2 patients expired from hepatic failure, 4/8(50%) patients with renal involvements progressed to chronic kidney disease(CKD) stage 2 or 3. 3 patients with CKD were diagnosed hepatorenal syndrome(HRS). Only 2(20%) patients have preserved their renal function without intervention.
Overall prevalence of renal involvement with ALGS in this study was 48%, exceeding previous report. Also, renal phenotypes were more diverse than reported. Especially the prevalence of NC/NL was notable, high as 2/10(20%), and 1 patient needed extracorporeal shockwave lithotripsy(ESWL). Since cystic kidney is a known risk factor for NC/NL, ALGS patients should be monitored for NC/NL concomitant with renal dysplasia. Moreover, watchful follow-up of renal manifestations in ALGS is necessary considering the portion of progression to CKD.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-014 - Prognosis in older children and adolescents with VUR and ROC analysis of eGFR as a predictor

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Background: It is well known that some vesicoureteral reflux (VUR) patients with renal impairment have a poor long-term prognosis. In addition, some patients retain renal function for a short period after surgery, but then decline. However, the prognosis for older children to adulthood is obscure.
Methods: Among VUR patients visited our center from 2007 to 2018, we compared the eGFR at the first and last visits of 77 patients who had been observed for more than 4 years and were at least 10 years old at the last visit.
Results: The sexes of 64 boys and 13 girls. The median age at the first visit was 2.0 years, at the last visit was 15.3 years, and the observation period was 11.8 years. 44 patients had bilateral VUR grade III or higher, and 63 had anti-reflux surgery. The eGFR (mL/min/1.73m2) was 75.6 at the first visit and 85.7 at the last visit, which was not significantly different, but 7 patients had progressed to CKD 5. We examined the cutoff value of initial eGFR to predict CKD 5 using the ROC curve, and found a relatively good predictive ability with an AUC of 0.812, cutoff value of 56.3, sensitivity of 75.0%, and specificity of 85.4%. However, 4 of the 32 CKD stage 2 cases developed CKD 5.
Discussion: This study showed that CKD 3 or higher at initial visit was a good cutoff value for predicting end-stage renal failure, which is important because therapeutic drugs for CKD are under development and early intervention is needed. However, some patients with mild renal dysfunction may develop renal failure and need careful monitoring. The present study was based on long-term observation case, so there was bias and the case number was small. Further study is needed.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-015 - Renal insufficiency in VACTER association; Single-center study

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A variety of renal anomalies are reported in 50-80% of VACTER association. Among them, a certain portion of patients develop chronic kidney disease (CKD) and frequently progress to end-stage renal disease (ESRD), requiring renal replacement therapy (RRT). This study is aimed to evaluate the clinical characteristic, prevalence, and risk factors of CKD in VACTER patients.

The medical records of pediatric (age 0-18 years) VACTER patients who visited Samsung Medical Center from January 2011 to December 2019 were reviewed retrospectively. This study used the traditional Schwarz formula to estimate glomerular filtration rate (eGFR) by serum creatinine (Cr). The CKD stage was classified according to Kidney Disease Improving Global Outcomes guideline, and CKD in this study was defined as CKD stage 2 to 5.

A total of 43 VACTERL patients were enrolled. Male was 1.9 times more predominant, and 88.4% of patients had renal anomalies (horseshoe kidney, hydronephrosis, multicystic dysplastic kidney, renal agenesis, renal dysgenesis, duplex, vesicoureteral reflux (VUR), ureteral anomalies, urethral anomalies bladder anomalies). The median follow-up period was 1.6 years, and the average eGFR was 138.0ml/min/1.73m2. Half of the patients had urinary tract infections (UTI), and 82% experienced UTI more than once. VUR was detected in 21 patients, and one-third of them underwent correction procedures. Eleven patients had prophylactic antibiotic medication, including nine patients with VUR. Six patients experienced acute kidney injury (AKI), and half progressed to CKD. One of the CKD patients required continuous renal replacement therapy and subsequently switched to peritoneal dialysis. In this study, the prevalence of CKD was 16.3%, and AKI increased the risk of CKD progression ten times. (p=0.0235)

The VACTERL has several factors which might influence renal insufficiency. However, in this study, solely AKI was proven to be a statistically significant risk factor of CKD. Further longitudinal studies of CKD in VACTER are required.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-016 - Clinical and Pathological Investigation of Oligomeganephronia

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Background: Oligomeganephronia (OMN) is a rare subtype of congenital anomalies of the kidney and urinary tract, characterized by decreased number and compensatory hypertrophy of the nephron. Hyperfiltration and excessive stress cause glomerular injury and glomerulosclerosis, with renal failure typically occurring in adulthood. It is caused by abnormal renal development during the embryonic period, especially in patients with fetal growth retardation and low birth weight; however, the actual etiology and clinical features are still unknown. Herein, we investigated cases diagnosed with OMN in our hospital to reveal the clinical and pathological characteristics, treatment, and outcome.

Methods: Ten patients pathologically diagnosed with OMN between 2013 and 2020 were retrospectively investigated. The data were presented as the median ± interquartile range, and statistical significance was set at $p < 0.05$.

Results: The age at diagnosis was 14.1 years, the male-to-female ratio was 6:4, and only four cases were born with low birth weight. The estimated glomerular filtration rate was 62.2 (58.5-64.6) mL/min/1.73 m^2 and the amount of proteinuria was 0.33 (0.22-0.66) g/gCre. The glomerulus diameter of OMN patients was significantly larger (217 vs 155 μm, $p < 0.001$) than the control group, and the number of glomeruli of OMN patients was lesser (0.89 vs 2.75 / mm^2, $p < 0.001$) than the control group. Eight of the ten cases were identified by urinary screening, and the remaining two cases were detected by incidental blood examination. Nine patients were treated with renin-angiotensin system (RAS) inhibitors, following which proteinuria successfully decreased or disappeared (0.080 (0.040-0.15) g/gCr).

Conclusions: As few symptoms can lead to OMN discovery, most patients were found during urine screening at school. Renal dysfunction was observed in all patients at the time of renal biopsy. Proteinuria was significantly reduced by RAS inhibitors, indicating their renoprotective effect.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-017 - The Role of Autotaxin in the Early Prediction of Progressive Renal Fibrosis in non-glomerular Chronic Kidney Disease in Children

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Background: Renal fibrosis (RF) is the pathological hallmark of chronic kidney disease (CKD) in congenital anomaly of the kidney and urinary tract (CAKUT). Single-kidney FUBI (Failure of Ureteric Bud Invasion) mice present progressive RF with CKD. In this study serial DNA microarray technology was used to identify molecular modulators of RF with ageing in single kidney FUBI mice. It was found that autotaxin (ATX) played an important role in RF of CAKUT.

Methods: Serial changes with ageing in single-kidney FUBI mice were investigated using microarray analysis. The identified candidate gene was validated using FUBI as well as UUO models and plasma samples from 146 CAKUT-CKD patients.

Results: Increased levels of ATX were found in FUBI mice where mRNA levels had been increased with ageing. The development of RF and renal ATX expression were both evident in the UUO model and from the progressive increase in the CKD stage determined by analysis of the plasma of CAKUT-CKD patients. It was found that ATX protein expression increased dramatically after the age of 12 months in single-kidney compared with double-kidney-FUBI mice and also increased with the progression of UUO-induced RF. ATX was absent in normal human renal tissue but was detected by immunohistology in human CKD renal dysplastic specimens. ATX induced collagen I, connective tissue growth factor (CTGF) and TGF-b1 protein expression were also evident in vitro in cultured. ATX induced renal CTGF expression was predominantly attributable to tubular epithelial cells. The knockdown of CTGF with siRNA also suppresses a-SMA mRNA expression by ATX stimulation on HRPTCs and it is clear that ATX-LPA-CTGF signaling makes an important contribution to the pathogenesis of RF in CAKUT-CKD.

Conclusion: The targeting of ATX-LPA-CTGF signaling could be a promising therapeutic strategy for RF, and ATX might serve as a novel tool for monitoring the progression of CAKUT-CKD.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-018 - Genetic spectrum of congenital anomalies of the kidney and urinary tracts and risk factors for kidney failure: A pediatric multicenter cohort study

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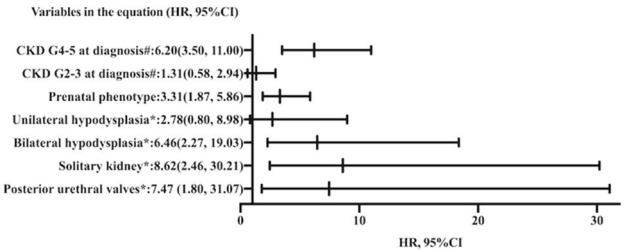
Rationale & Objective: Congenital anomalies of the kidney and urinary tracts (CAKUT) are the leading cause of kidney failure in children with phenotypic and genotypic heterogeneity. The objective of this study was to describe the genetic spectrum of CAKUT and identify the risk factors for kidney failure in children.
Study Design: Retrospective cohort study.
Setting & Participants: Clinical, anatomical, and genetic data were derived from a multicenter registration network (Chinese Children Genetic Kidney Disease Database, CCGKDD), and the Chigene database. This analysis included 925 CAKUT children who underwent genetic tests in 2014 to 2020. 584 of 925 children were from CCGKDD, with longitudinal data for kidney function.
Exposure: Different clinical, anatomical, and genetic entities.
Outcome: Kidney failure.
Analytical Approach: The kidney survival as well as the median (95% confidence interval) time to kidney failure was estimated by the Kaplan-Meier method. Analysis of the association of kidney failure, with the exposure of interest was conducted by Cox proportional hazards model.
Results: A molecular genetic diagnosis was established in 96 out of 925 (10.3%) children. Genetic diagnosis rate varies among different anatomical catalogues. Eighty-two patients from CCGKDD progressed to kidney failure at the median age of 13.0 (95% confidence interval, 12.4-13.6) years. Patients with variants of *PAX2, TNXB, EYA1, HNF1B, GATA3,* 48,XXYY showed worse outcomes (X^2=18.0, P <0.001). Multivariate analysis indicated solitary kidney, posterior urethral valves, bilateral hypodysplasia, CKD stage 4-5 at diagnosis and prenatal diagnosis were independent prognostic factors in children with CAKUT. Patients with genetic diagnosis and extrarenal diagnosis predicted shorter kidney survival in crude analysis but not in adjusted models.



Limitations: Missing data, and relatively small sample size.
Conclusions: Genetic diagnosis rate varies among different anatomical catalogues. Sub-clinical defects of CAKUT have a more significant impact on prognosis than genetic test results and extrarenal diagnosis.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-019 - Rare kidney disease management at University Medical Centre Maribor

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Background: Despite their low prevalence, rare kidney diseases (RKD) must be treated with the same professional approach as common diseases. The research aimed to analyse the data of patients with RKD, managed at the University Medical Centre Maribor.
Methods: The research was conducted in 2021 with our data entered in the ERKReg and in the hospital informational system. Basic patient data (age, sex, clinical diagnosis, year of diagnosis), creatinine values, stage of chronic kidney disease (CKD), the presence of hypertension, and patient's medications were collected and analysed.
Results: 126 patients (58 women, 68 men) with RKD were included in the study. The most common groups were congenital anomalies of the kidneys and urinary tract (CAKUT) with 62.7% of patients, followed by glomerulopathies with 17.5% and familial cystic renal diseases with 13.4%. All other groups accounted for less than 10% of patients. The most common diagnosis was vesicoureteral reflux, present in 28.3% of the cases, diagnosed on average at the age of 1.5 years, while in other disease groups between the age of 8 and 9 years. The mean creatinine value in patients with CAKUT at diagnosis was 53 µmol/L, with no deterioration after five years. Most patients had grade one CKD (63%), followed by stage two in 36%. Less than 1% of all patients had grade five CKD. 10% of all patients were diagnosed with hypertension, and half were successfully treated with one antihypertensive medication. The most common indication for surgical treatment was vesicoureteral reflux, followed by pyeloureteral stenosis, and 33% of patients required surgery.
Conclusions: The study found that the prevalence of children with RKD in the Podravska region is higher than the predicted prevalence in Europe, with a highly asymmetric distribution of individual diseases. Hypertension is present in 10 % and stage one CKD in 63%.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-021 - Extrinsic ureteo-pelvic junction stenosis in children with hydronephrosis caused by crossing lower pole vessels

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Accessory renal arteries are routinely considered to be normal anatomical variant.
However, lower pole renal vessel (CV) crossing ureter subpelvically may be the cause of pediatric ureteropelvic junction obstruction (UPJO).
The aim of the study was to analyze lower pole renal vessel, subpelvically crossing the ureter as a cause of extrinsic ureteo-pelvic junction stenosis in children with hydronephrosis.
Material and Methods: Group of 77 children diagnosed with UPJO was involved into the study, 50 males (65%), median age 29 (4-108) months; Left kidney 62%.
Color doppler ultrasound (CD-US) of renal arteries was performed in 44 patients (57%) using Aloka Prosound alpha 6, convex transducer 2-6 MHz. Diuretic renography was used to determine renal function.
In remaining 33 pts (43%) doppler assesement of renal vessels was not available.
Results: In CD-US 16 from 44 patiets (36,4%) was found with accessory vessel crossing (CV) the ureter subpelvically, causing UPJO, median age 108,5 (69-159) months; 5 female, 11 male (69%).
In this CV –group first diagnosis of hydronephrosis was set at the age of 105 (31-162), in prenatal diagnostics in 2 children; 8 children complained of abdominal pain (50%). There were 5/16 early divisions of renal artery, 11/16 accessory renal artery to the lower pole of the kidney.
28/44 children without crossing vessel were significantly younger, median age 10 (4-89,5) months, with earlier diagnosis of hydronephrosis, at median age of 6 months (0-111)- in 5 in prenatal period; 4 children (14%) presented with abdominal pain.
In dynamic renal scyntigraphy there was no differece in reaction to Furosemide in children with or without crossing vessel.
Conclusions: Extrinsic UPJO was found in 36,4% of examined patients. In older children the incidence of extrinsic UPJO was higher. CD-US is a useful and sensitive method to detect crossing vessel in UPJO, and should be considered as the investigation of choice in children with hydronephrosis.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-022 - Early predictive factors for progression to kidney failure in patients with severe congenital anomalies of the kidney and urinary tract (CAKUT): a multicenter retrospective cohort study in Japan

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Background: Severe congenital anomalies of the kidney and urinary tract (CAKUT) progresses to infantile kidney failure with replacement therapy (KFRT). Although prompt and precise prediction of kidney outcome is important, early predictive factors for its progression remain unknown.
Methods: This retrospective cohort study included patients with CAKUT treated at 12 centers between 2009 and 2020. Patients with a maximum serum creatinine (SCr) level ≤1.0 mg/dL during the first 3 days, patients who died of respiratory failure during the neonatal period, patients who progressed to KFRT within the first 3 days, and patients lacking sufficient data were excluded.
Results: Of a total of 2187 patients with CAKUT, 92 patients were finally analyzed. Twenty-five patients (27%) progressed to KFRT and 24 (26%) had stage 3−5 chronic kidney disease without replacement therapy during the median observation period of 52 (1−139) months. Among these, 22 (24%) progressed to infantile KFRT. The kidney survival rate during infantile period was significantly lower in patients with a maximum SCr level during the first 3 days (Cr-day3-max) ≥2.5 mg/dL (21.8%) compared with those with a Cr-day3-max <2.5 mg/dL (95.2%) (log-rank, $P < 0.001$). Multivariate analysis identified Cr-day3-max ($P < 0.0001$) and oligohydramnios ($P = 0.04$) as associated with higher risks of infantile KFRT. Eighty-two patients (89%) were alive at last follow-up.
Conclusion: Neonatal kidney function, including Cr-day3-max, was strongly associated with kidney outcome in patients with severe CAKUT. Aggressive therapy for severe CAKUT may have good long-term outcomes through infantile dialysis and kidney transplantation.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-023 - Bladder wall-renal cortical index and renal outcome in patients with a posterior urethral valve

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Abstract
Posterior urethral valve (PUV) is the commonest congenital anomalies of the kidney and urinary tract (CAKUT) in boys. It is associated with increase mortality and morbidity consequent on bladder dysfunction and renal complications. Serum creatinine; the most available maker of kidney function is an unreliable long term predictor of renal outcome.

A reliable index to predict the renal outcome is required to guide care and predict future evaluation and active management frequency. This study presents a preliminary report of bladder wall- cortical index and subsequent renal outcomes of children with PUV in tertiary centre Southwestern Nigeria.
Methods: This is a prospective study of children with PUV seen between March 2015 and May 2016. Descriptive analysis of patients' demographic and clinical characteristics was undertaken. Using a 3-5 MHz curvilinear probe and a 7-11 MHz linear probe, the kidneys were measured for size and parenchymal echopattern in all planes, as well as renal cortical thickness. The bladder wall thickness was measured from the interface of urine and internal mucosa to the outer part of the hypoechogenic muscular layer. The estimated glomerular filtration rate at diagnosis and at 2 years follow up was compared with the bladder wall thickness and renal cortical thinness index at first contact. Data were analysed using GraphPad Prism 9.
Results: The cohort's median age was 5 months (range 3days -11 years, IQR 1.0, 24.0months). The most frequent clinical features included: poor urinary stream, lower abdominal swelling and breathlessness. PUV was complications with urinary tract infections, vesicourethral reflux disease, Acute Kidney Injury (AKI), proteinuria and failure to thrive. The bladder-wall-renal cortical index at recruitment was associated with lower eGFR and increased mortality at 2 years of follow up.
Conclusion: PUV was associated with increased morbidity and mortality. Bladder wall thickness-renal cortical thinness index was associated with lower eGFR and mortality at 2years.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-024 - Clinico-radiological profile and outcomes of antenatal hydronephrosis from a tertiary care center in a developing country, Addressing the management dilemmas

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Introduction: Routine antenatal ultrasound examinations have resulted in the increased detection of congenital anomalies of kidney and urinary tract. Antenatal hydronephrosis (ANH) is the most common amongst them with a prevalence of 0.5-5%. Though its transient in 41-88% cases and resolves spontaneously, about 4-15% require some postnatal intervention. Our aim is not to miss significant pathological conditions, but at the same time avoid over evaluation and treatment of minor abnormalities, especially in resource limited setting thus living by our ethics of beneficence and nonmaleficence.
Objectives: 1. To study the clinico-radiological profile of infants with antenatal hydronephrosis and time to resolution in different grades of hydronephrosis.
2. To study the outcomes of antenatal hydronephrosis in infants at 3, 6,12 and 18 months of follow up.
Methodology: 120 infants with antenatal hydronephrosis were prospectively followed up till 18 months of postnatal age. Findings of antenatal scans were recorded and infants were divided into three groups as mild (APD <10mm), moderate (APD 10-15mm) severe (APD > 15mm) based on the grade of hydronephrosis on the ultrasound in first week of life. Statistical analysis was performed to find the relationship between the grade of hydronephrosis with antenatal scans, association with urinary tract anomalies, mean time to resolution, episodes of urinary tract infections, benefit of antibiotic prophylaxis, frequency of imaging such as renal dynamic scans (RDS) and micturating cystourethrogram (MCU) and significant surgical interventions.
Results: Mild hydronephrosis was present in 50-60% of the cases which resolved at 6 months of postnatal age, whereas moderate to severe variety persisted beyond 9-12 months. Postnatal imaging within first week and at 6 weeks were better predictors of the outcomes as compared to the antenatal scans. Only 5-8% of the total cases required surgery and 3-7% had UTI. Results at 18 months follow up would contribute to the median follow up required in such patients.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-025 - GEN1 is likely to be a causative gene of human CAKUT

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Background: CAKUT refers to a series of diseases that contain anatomical abnormalities of the urinary system, with an incidence of up to 3-6/1000 in newborns worldwide, and is the leading cause of end-stage kidney disease in children. Based on the summary of previous studies, single-gene etiology accounts for 18% of the CAKUT etiology that can be found by the current technology. In our previous studies, the mice with mutations caused by the insertion of GEN1 with PB transposons have similar phenotypes consistent with CAKUT patients. However, whether GEN1 is the causative gene of CAKUT in human is unknown.
Objective: To verify whether GEN1 is the pathogenic gene of human CAKUT that broaden the gene pool of CAKUT in human.
Methods: We collected CAKUT children who had GEN1 variants without known CAKUT-causing genes, analyzed the amino acid conservatism, constructed missense mutation plasmids, transfected 293T cells to observe the GEN1 gene and protein expression, and identified the stability of the mutant proteins. After purified mutant proteins, their basic functions were detected, including enzyme activity and the binding ability to DNA. The splicing function of a splicing near site mutation was detected at the same time.
Results: A total of 32 children with GEN1 variation were found in 785 children, including 25 children with CAKUT and 7 children without CAKUT. A total of 460 patients with CAKUT were found in 785 patients (α=0.025, χ^2 =5.24, P<0.05). The enzyme activity and binding ability of the purified missense mutant proteins decreased uniformly to varying degrees relative to the wild-type protein, of which p.R401X, 508 decreased significantly. In protein stability experiment, the p.R401X, 508 was the most unstable. In minigene splicing experiment, an abnormal splicing occurred in mutation c.1071+3 (IVS10) A >G, formed a shorter exon 10.
Conclusion: In the sequenced population, the study indicated that GEN1 was correlated with CAKUT. The mutant GEN1 proteins have damaged functions compared with wild-type GEN1 protein in vitro.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-027 - Congenital dilation of the urinary tract: prognostic value of ultrasound grading systems

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Urinary tract dilations represent one of the major anomalies detected at prenatal ultrasound screening. To date, there is a lack of uniformity in the use of ultrasound grading systems.
The objective of this study was to analyze the correlation between antenatal dilation degree, according to UTD and SFU grading systems, and postnatal clinical outcomes.
A retrospective analysis was performed on 94 cases with prenatal diagnosis of urinary tract dilation from 2013 to 2020. All patients were classified according to prenatal SFU (mild, moderate, severe) and UTD grading system (A1, A2-3). The analyzed endpoints were spontaneous resolution of dilations, vesico-ureteral reflux (VUR) and urinary tract infections (UTI). For both classifications low-risk grades ("mild" and A1) correlated significantly with spontaneous resolution of dilation (respectively 55% and 58%, $p < 0.001$). The "severe" SFU grade appeared to be significantly associated with the diagnosis of VUR with an OR=24.89 (p-value=0.004); instead UTD grade A2-3 association was not statistically significative. On the other hand, in relation to UTIs, there was a more significant correlation with the severe SFU grade, compared to the UTD A2-3 grade: for the severe SFU grade an OR=14.55 (p-value=0.02) was calculated. From the comparison of the two classification systems using ROC curves, SFU grading seemed to have higher accuracy than UTD classification for the prediction of VUR (respectively AUC 0.827 and 0.683) and UTI (respectively AUC 0.767 and 0.673). Analyzing spontaneous resolution, an AUC of 0.745 for SFU and 0.725 for UTD grading was calculated.
Both SFU and UTD grading system appeared to be useful tools for the management of prenatal urinary tract dilations. In our sample SFU system seemed to have higher accuracy than UTD classification for the prediction of VUR and UTI. More studies are needed, including postnatal classifications and other endpoints, with larger population and longer follow-up.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-029 - Posterior urethral valves in Children: Challenges of management at the University of Port Harcourt Teaching Hospital, Nigeria

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Introduction: Posterior urethral valve (PUV) is the commonest obstructive uropathy seen in children in our hospital. However, it's management is fraught with a lot of challenges in our environment with resultant poor outcome due to late presentation, financial constraints and unavailability of facilities for surgical resection.
Aim: To highlight challenges in management and outcome of patients presenting with posterior urethral valves at the University of Port Harcourt Teaching Hospital over a 3year period.
Methods: The renal forms of all children with renal disease and those with the diagnosis of posterior urethral valves seen at the Paediatric Nephrology unit from June 2019 to April 2022 were reviewed. The relevant information regarding the clinical presentation, management and outcome of those with PUV were retrieved and analysed.
Results: Out of 167 renal cases seen, 20(12%) had PUV. The age range was 1day to 12years with a mean age of 2.17 ± 2.95 yrs. Prenatal diagnosis was made in 2(10%) patients. Seven (35%) presented in the neonatal period while 8(40%) presented after 6months. The most common presentation was dribbling of urine in all patients (100%) and fever in 10 (50%). The common complications were urinary tract infection in 16(80%) and uremia in 10(50%). Four (20%) patients had transvesical excision of valves after one year of life and 1(5%) had vesicostomy. None had transurethral valve resection. The mean initial serum creatinine at presentation was 277.35 ± 194.17umol/l and 159.57 ± 146.15umol/l post intervention (continuous bladder drainage/surgery). Seven patients (36.8%) had end stage renal disease (ESRD). Five (25%) signed against medical advice and mortality rate was 25%.
Conclusion: Prenatal diagnosis of PUV is very low in our environment, while transvesical valve excision is the common method of surgical repair due to unavailability of infant resectoscope. The morbidity and mortality rates are high due to these challenges in the management.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-030 - Prediction of mortality in fetuses with renal oligohydramnios using antenatal and early postnatal parameters

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Introduction: Renal oligohydramnios (ROH) is caused by bilateral congenital abnormalities, either of renal parenchymal or obstructive origine. ROH is a poor prognostic factor of neonatal survival, lung hypoplasia being the main cause of mortality. However, the short or medium prognosis is highly variable. We aimed to describe the fetal morbidity and mortality in case of renal oligohydramnios due to renal congenital pathologies and to find predictive risk factors for morbidity and mortality.
Patients and Methods: Observational retrospective single center study. All data were collected in Trousseau Hospital in the department of gynecology-obstretric, neonatology and pediatric nephrology, from March 2008 to September 2020.
Results: We included 66 foetuses with renal parenchymal pathologies or posterior urethral valves causing oligamnios or anamnios, identified on antenatal ultrasound or at childbirth, who have not had a premature rupture of the membranes during pregnancy. Total mortality was 75% (50/66) including 35% antenatal deaths (22 terminations of pregnancy and 1 intrauterine death), 10 died immediately after birth, 17 died in neonatal intensive care unit and 16 survived. The presence of pneumomediastinum and pneumothorax was not different in survivors and non-survivors.
Regarding antenatal characteristics, foetuses with kidneys having a sonographic aspect of hypodysplasia at T2 and an anamnios or oligohydramnios before 24 weeks GA had a higher risk to die, often due to lung hypoplasia. Mortality was correlated with the severity of kidney damage. There was a significant difference in plasma creatinine in the surviving patients compared to the deceased patients, from day 3 onwards (183 µmol/L [88; 255] versus 295 µmol/L [247; 326]; p=0.038).
Conclusion: The presence of pulmonary hypoplasia was frequent but did not appear to be associated with an increase of neonatal mortality. However, the severity of early renal dysfunction (from day 3 onwards) and bilateral dysplasia detection on ultrasound before 24 weeks GA were correlated with mortality.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-031 - Diagnostic yield and benefits of whole-exome sequencing in patients with congenital anomalies of the kidney and urinary tract (CAKUT) diagnosed in the first thousand days of life

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Congenital anomalies of the kidney and urinary tract (CAKUT) are the predominant cause of chronic kidney disease (CKD) in children and adolescents. Although over 50 genes are known to cause CAKUT if mutated, the diagnostic yield of whole-exome sequencing (WES) in heterogeneous CAKUT cohorts is typically lower than 15%. Here, we asked for the diagnostic yield in a defined CAKUT cohort, i.e. patients diagnosed before the age of three years, and whether an early genetic diagnosis may impact patient management. In 100 patients diagnosed with CAKUT in the first 1,000 days of life, WES was performed, and variants in 58 established CAKUT-associated genes were extracted and classified according to the ACMG guidelines. The translational value of the genetic findings was assessed. In 25% of patients, we identified a rare likely pathogenic (LP) or pathogenic (P) variant in one or two of 15 CAKUT-associated genes, including *LIFR*, *PAX2*, *SALL1, SIX2,* and *TBC1D1,* playing a role in nine different molecular pathways, including GDNF/RET and WNT signaling. Of the 27 different variants detected, 52% were loss-of-function and 19% *de novo* variants. In 21 of the 25 (84%) patients carrying a LP/P variant, a gene was affected that was previously associated with specific extrarenal anomalies, allowing an earlier diagnosis and treatment of (subclinical) comorbidities including prediabetes, hyperuricemia and hypoparathyroidism in 10/100 patients. CAKUT patients requiring kidney replacement therapy (KRT) before the age of three years and those presenting with extrarenal anomalies had a significantly higher likelihood to carry LP/P variants (odds ratio 2.95 or 3.5, respectively). Altogether, we demonstrate a comparatively high diagnostic yield of WES in children diagnosed with CAKUT in infancy, particularly in those requiring KRT or presenting with extrarenal anomalies, and suggest a benefit for earlier management of comorbidities. (Funding: Else Kröner-Fresenius-Stiftung, grant no. 2018_Kolleg.12; Deutsche Forschungsgemeinschaft, grants no. KO5614/2-1, MA9606/1-1)

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-032 - Incidence and follow-up of antenatally detected congenital anomalies of the kidneys and urinary tract in a tertiary neonatal unit

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Introduction: Congenital anomalies of the kidney and urinary tract (CAKUT) are the most common cause of end-stage renal failure in children. There is a well-established causative relationship between CAKUT and the requirement for renal replacement therapy, which carries significant health and psychosocial burden for families. With an overall incidence of 0.3-1.6 per 1000 births, CAKUT constitutes up to 30% of all anomalies detected in the prenatal period. This audit was conducted to ascertain our performance in managing CAKUT, thereby minimising the degree of renal damage and preventing progression to end-stage renal failure.
Methods: A retrospective chart review was performed of all patients with antenatally detected renal anomalies at the Rotunda Hospital from March 2020-March 2021. Powerchart and NIMIS records were used for data collection.
Results: A cohort of n=65 patients were identified, of which two transferred care to an alternate centre prior to delivery and were excluded. n=63 patients were included, 38 (60.3%) were male and 25 (39.7%) were female. The mean gestational age at initial detection of CAKUT was 24.87 weeks (IQR 20-32). n=26 (41.27%) of patients had a proven diagnosis of CAKUT. The most prevalent anomaly was hydronephrosis, with n=19 patients investigated for this. Of patients with antenatally diagnosed hydronephrosis, 63.2% of scans specified renal measurements. Our institution's percentage compliance with guidelines was 89.65%. Adherence to guidelines was poorest in the domains of bilateral hydronephrosis and ectopic kidneys (0% and 50% respectively). Four terminations of pregnancy were noted and six patients died in the perinatal period.
Conclusion: CAKUT are common in the practice of both Obstetricians and Neonatologists. It is important to include renal measurements in ultrasound reports, where hydronephrosis is concerned to facilitate timely and accurate post-natal management. Though our compliance with best-practice guidelines was high, Neonatologists must ensure post-natal imaging is conducted in an appropriate time-frame.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-033 - Single-center analysis of the incidence of fetal congenital anomalies of kidney and urinary tract diagnosed by intrauterine three-dimensional ultrasonography

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Objective: Congenital anomalies of kidney and urinary tract (CAKUT) is an important cause of chronic kidney disease and end-stage renal disease in children. This study investigated the occurrence of intrauterine CAKUT in our hospital through prenatal ultrasound examination, so as to help the early detection of the disease .

Methods: Three dimensional ultrasonography was performed on pregnant women registered in fetal Medical Center of our hospital from December 2009 to December 2019. The incidence of intrauterine CAKUT was analyzed.
Results: A total of 79232 cases of pregnant women underwent prenatal ultrasound examination were counted, among which 957 cases were found to have urinary CAKUT in the fetal urinary system by prenatal ultrasound examination, with an incidence of 1.21%. 697 patients with pyelectasis , renal cystic disease in 82 cases, 46 cases of renal agenesis, 32 cases of ectopic kidney, duplication of renal pelvis and ureter in 34 cases, 5 cases were horseshoe kidney, simple renal dysplasia in 5 cases, pyelectasis with renal cystic disease in 1 case, pyelectasis with duplication of renal pelvis and ureter in 1 case, renal cystic disease with horseshoe kidney in 1 case, renal cystic disease with renal agenesis in 1 case, renal cystic disease with ectopic kidney in 1 case, renal dysplasia with renal agenesis in 1 case, renal dysplasia with duplication of renal pelvis and ureter in 1 case, 1 case of ectopic kidney with duplication of renal pelvis and ureter, renal parenchyma medulla echo abnormal 31 cases, renal vascular dysplasia in 5 cases, 9 cases of bladder dysplasia and ureteral dysplasia in 3 cases.
Conclusion: The incidence of intrauterine CAKUT in single center of our hospital was 1.21%. The common types were as follows: pyelectasis, renal cystic disease , renal agenesis , duplication of renal pelvis and ureter, ectopic kidney. The incidence was 72.83%, 8.57%, 4.81%, 3.55%, 3.34% respectively.

Congenital abnormalities of the Kidney and Urinary Tract (CAKUT)

P1-035 - Urine biomarkers and reflux nephropathy (RN) In children with vezico-renal reflux (VUR).

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The available modern diagnostic methods often do not allow to establish the initial structural and functional changes of the kidneys. 99mTc-DMSA renal scan reveals fibrous foci that have already formed, and does not allow detecting initial and potentially reversible fibrous changes. Therefore, there is a need to develop sensitive methods for early diagnosis of kidney damage, inflammation and fibrosis.
The aim was to evaluate the relationship between urine biomarkers and renal scarring in children with VUR.
Method: 117 patients aged 3 to 16 years (mean age 10.2 ± 4.5, 70.1% of girls) with VUR were examined. The control group consisted of 40 healthy children. All children underwent a complete nephrological examination. The levels of transforming growth factor (TGF-β1) and angiotensin II (Ang II), microalbumin (MA) were determined in morning urine using the ELISA method. To identify the severity of the lesion of the renal parenchyma, a static DMSA scan was performed. According to DMSA, the children were divided into 3 groups: 1 gr. – VUR without signs of sclerosis (15.4%), 2 gr. – VUR+1-2 foci (44.74%) and 3 gr VUR+ > 3-4 foci of sclerosis (40.1%). All patients with VUR had a high urinary excretion of all biomarkers when compared with the control group ($p<0.05$). The concentrations of all urine biomarkers were significantly higher in the gr.2 and gr.3 than gr.1 ($p<0.0001$). TGF-β1, Ang II and MA were correlated with renal scars. The same urine biomarkers also correlated with GFR.
Conclusions: DMSA renal scan, showed a direct correlations with the severity of VUR. We established a reliable dependence of the excretion biomarkers in the urine on the severity of RN according to DMSA scan in children with VUR. The excretion of biomarkers in the urine as non-invasive markers can be used as a criterion for the development and progression of nephropathy in VUR.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-036 - Renal Cysts and Diabetes Syndrome – An entity where thorough family history often points towards the diagnosis

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Introduction: *HNF1B* haploinsufficiency is associated to Renal Cysts and Diabetes Syndrome (RCAD-MIM#137920), an entity with autosomal dominant transmission. It may be caused by heterozygous single nucleotide deleterious variants or whole-gene deletions, the later within a recurrent 17q12 deletion locus. There is a wide array of associated kidney manifestations, most frequently cysts.
Case Series: We present four (one girl, three boys) pediatric patients, aged one to 15 years, from three families with pathogenic *HNF1B* variants, two of which with the 17q12 recurring deletion. All 4 patients presented renal abnormalities, with cystic kidney as first finding in three of them. One had prenatal pyelectasia, which improved over time. Both patients with the recurring deletion presented dysmorphic features. One presented developmental delay, and the other functional liver abnormalities and congenital heart disease. Diagnosis was made through 17q12 MLPA assay in one family, CGH-array in one family, and WES-based gene panel for kidney disease in the other. Careful inquiry in genetics consultation had identified family history in 2 of the families, with suggestive findings spanning over 4 generations in one of the families, and 2 in the other. Diabetes and renal cysts were simultaneously present in 2 adults.
Discussion: RCAD is a multisystemic disorder with kidney disease being the most common and often the inaugurating feature. RCAD is an important diagnosis to consider in the presence of pediatric kidney disease, particularly when family history includes diabetes cosegregating with kidney disease in an autosomal dominant pattern. Genetic diagnosis is paramount, as it prevents invasive diagnostic procedures, directs follow-up and treatment, and allows adequate genetic counselling for patients and families.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-037 - A novel frameshift homozygous mutation in FAT1 gene causes ptosis, nephropathy and syndactyly in Emirati family: case report and literature review

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Single gene mutations are important causes of glomerular disease in children. Of these genes, mutations in *FAT1* gene have been recently described in the literature as a cause of nephropathy in isolated form or multi-system involvement. The spectrum of renal disease associated with *FAT1* gene mutations is variable ranging from asymptomatic proteinuria and hematuria to severe nephrotic syndrome and end-stage renal disease. In this case report, we describe a 3 year-old child along with two other family members with a novel frameshift homozygous mutation in *FAT1* gene consistent with the diagnosis of autosomal recessive colobomatous-microphthalmia, ptosis, nephropathy and syndactyly syndrome with variable expression of phenotype. This report adds to the genotype-phenotype correlation, highlighting the clinical importance of considering *FAT1* gene defects as part of the differential diagnosis for congenital ptosis, syndactyly and nephropathy especially with multiple affected family members.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-040 - Isolated kidney transplantation under lumasiran therapy in primary hyperoxaluria type 1 (PH1): a report on 3 cases

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Objectives: The RNA-interference therapy lumasiran demonstrated its efficacy to decrease urinary (UOx/creat) and circulating (POx) oxalate levels in PH1. Whether combined liver/kidney transplantation (CLKTx) can be replaced by isolated KTx and lumasiran remains debatable.
Methods: Three cases of genetically-confirmed PH1 patients receiving isolated KTx are described. They all received post-operatively "standard of care" (SOC), associating hyperhydration (3L/m²/day), potassium citrate (250mg/kg/day), pyridoxine and lumasiran.
Results: Patient 1: diagnosis 1.5 years, dialysis initiation 0.5 years, POx 110µmol/L (N<5) at the beginning of lumasiran at 2.5 years, KTx 13 months after lumasiran (POx 53µmol/L), deceased donor. Post-operative management: 3 early "prophylactic" hemodialysis sessions, then SOC. ARF on JJ obstruction at day 5, 15 hemodialysis sessions. At one month, renal function 125mL/min/1.73 m², POx 14µmol/L, UOx/creat 519µmol/mmol (<100). Follow-up 3 months, stable renal function, POx and UOx/creat.
Patient 2: diagnosis 17 years, dialysis initiation 23 years, POx 20µmol/L at the beginning of lumasiran at 26 years, KTx 10 months after lumasiran (POx 10µmol/L), living donor. No delayed graft function. Post-operative management: SOC. At one month, renal function 48mL/min/1.73 m², POx<5 µmol/L, UOx/creat 67µmol/mmol (<80). Follow-up 3 months, stable renal function and normal UOx/creat.
Patient 3: diagnosis 6 years, dialysis initiation 12 years, POx 128µmol/L at the beginning of lumasiran at 17 years, KTx 17 months after lumasiran (POx 23µmol/L), deceased donor. No delayed graft function. Post-operative management: SOC. At one month, renal function 50mL/min/1.73 m², POx 28µmol/L, UOx/creat 245µmol/mmol (<80). Arterial thrombosis post-lymphocele 41 days post KTx, requiring 13 daily hemodialysis sessions. Follow-up 3 months, renal function 50mL/min/1.73m² and stable UOx/creat.
Conclusion: We report the first successful isolated KTx in PH1 patients under lumasiran. Long-term data are obviously required. As described in CLKTx, post-operative hyperhydration and alkalinization is crucial, as long as urinary oxalate remains elevated from bone release.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-041 - A case of nephrotic syndrome caused by COQ6 gene mutation with significant podocyte hypertrophy

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Backgrounds: Genetic caused has been identified in nearly one third of pediatric steroid-resistant NS (SRNS). Hereditary coenzyme Q10 deficiency can lead to nephrotic syndrome, through reversable mitochondrial disorder. According to previous report, the patients would benefit from early CoQ(10) supplement and reach complete remission.
Case: A 10-month-old boy presented with edema, nephrotic proteinuria and hypoalbuminemia. Meanwhile he was found with HBV infection. The parents are not consanguineous, without a family history of glomerulopathy. On admission, physical examination showed the baby had severe general edema. Hemofiltration and peritoneal dialysis were initiated sequentially, due to no improvement after albumin and diuretics infusion. Renal biopsy was performed in the 6th week from disease onset. Diffuse mesangial sclerosis were found on light microscopy. By electron microscopy, hypertrophic podocytes were found, with a large number of mitochondria accumulated in podocytes. Staining of HBsAg and HBc-Ag were negative. After gene testing, two heterozygous pathogenic variants in COQ6 gene were identified in the patient. One was c.782C>T (p. Pro261Leu) inherited from his father, which had been reported before. Another was a deletion of exon3 and exon4 inherited from his mother, which was novel. After 6 weeks of CoQ(10) supplement, urinary protein/creatinine ratio declined, with serum albumin level raised. High dose CoQ10, 30mg/kg/d, were prescribed empirically with antiviral therapy. Three months later, the dose of CoQ(10) was adjusted to 50mg/kg/d.
Conclusions: In this case, nephrotic syndrome was caused by recessive COQ6 gene mutation. The case was characterized by podocyte hypertrophy and mitochondria accumulation. So far, proteinuria partially benefited from CoQ(10) supplement. Effectiveness of higher dose of CoQ10 needs to be identified during further follow up.
Points of discussion: To explore the significance of renal pathology in early detection of COQ6 gene mutation caused nephrotic syndrome. To disccuss the dose and efficacy of CoQ10 supplement.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-042 - Renal comorbidities in pediatric XLH patients in the German XLH registry / cohort study

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Objectives: X-linked hypophosphatemia (XLH), the most frequent hereditary cause of hypophosphatemic rickets, is due to mutations in the *PHEX* gene which results in elevated circulating levels of fibroblast growth factor 23 (FGF23), consecutive renal phosphate wasting and rickets. Patients are at risk for development of nephrocalcinosis which is thought to be mainly due to conventional treatment with active vitamin D metabolites and phosphate. Detailed analysis on renal health and its contributing factors in XLH patients are lacking.
Methods: We started a German registry and cohort study that is planned for ten years to investigate renal and other comorbidities in children with XLH treated with conventional therapy or burosumab, a fully humanized anti-FGF23 antibody. Detailed clinical and biochemical data as well as urine samples are annually obtained to assess urinary lithogenic substances and their associations e.g. with estimated glomerular filtration rate (eGFR) and nephrocalcinosis.
Results: Currently, 89 patients (56 girls, mean age of 8.8 ± 4.3 years) from 23 different centers are included in the study. 15% of patients have been treated conventionally for 11.5 ± 4.9 years, and 85% of patients have received burosumab for 3.6 ± 0.8 years with 5.9 ± 4.3 years of conventional therapy beforehand. A reduced eGFR (<90 ml/min/1.73m^2) and/or nephrocalcinosis was noted in 7% and 29.4% of patients, respectively. So far, detailed urine analysis is available in 57 patients (56 treated with burosumab, 1 treated conventionally) demonstrating hyperoxaluria (22.8%), hypercalciuria (16%), hypocitraturia (12.3%), and/or hyperglycolaturia (1.8%). The patient under conventional therapy showed hyperoxaluria, whereas the other lithogenic substances were on a normal level.
Conclusions: In this real-world study children with XLH presented with considerable renal comorbidity including reduced eGFR, nephrocalcinosis and elevated urinary lithogenic substances. The relative contributions of conventional and burosumab treatment will be clarified in the further course of our prospective registry.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-043 - Safety of stiripentol, where do we stand?

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Background: Stiripentol is marketed since 2007 as anti-seizure therapy in Dravet syndrome, a rare and severe infantile epilepsy. Because stiripentol is currently investigated for treating patients with primary hyperoxaluria (PH), we ought to describe available information regarding its safety in children, notably with renal insufficiency.
Methods: We extensively reviewed available safety information of stiripentol in the summary of product characteristics, in pharmacovigilance databases, and in the literature.
Results: Safety data spans 25 years and includes patients from 6 months to adulthood. When prescribed by neuropaediatricians, stiripentol is associated to other anti-seizure medications, mostly sodium valproate and clobazam. Overall, 438 unique Dravet patients received stiripentol during clinical trials, and only one episode of nephrolithiasis considered as not related to stiripentol was reported. Similarly, no renal adverse events (AEs) were observed in 18 patients (3 PH, 1 with kidney calculus, 14 Dravet Syndrome) with a renal history who received stiripentol.
The post-marketing estimated cumulative exposure to stiripentol is 45,131 patient-year. The most commonly reported AEs primarily affect the central nervous system (e.g somnolence) and the gastrointestinal tract (e.g. decreased appetite, vomiting). Whether these symptoms are secondary to stiripentol, to associated treatments or to the primary epilepsy remains to be determined.
Recently, safety data were collected during the HYPOP pilot trial (NCT03819647) evaluating stiripentol monotherapy in patients with PH. Among the 10 children (1-19 years) recruited, no renal adverse events were reported and the only AE considered related to the study treatment was an episode of "decreased appetite". Finally, among the 7 published case reports describing the 8-week to 20-month compassionate use of stiripentol in PH1 patients (aged 6 weeks to 17 years), no adverse events were reported.
Conclusions: Clinical safety data suggest that stiripentol neither induces adverse effect in the renal system, nor triggers unexpected adverse events in patients with renal disorders. This information warrants further investigations in clinical studies.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-044 - Sex differences of Burosumab in children with X-linked hypophosphataemic rickets

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Background: X-linked hypophosphataemic rickets (XLH) affects males more severely than the heterozygous females. However, the fully

humanized monoclonal antibody against fibroblast growth factor 23 (burosumab) has the same paediatric dose recommendation for both sexes (0.8 mg/kg every 2 weeks).

Patients and Methods: We describe burosumab response differences by sex in a case series of children with XLH. We analysed available data from the electronic medical records of all cases, using descriptive statistics.

Results: We treated 10 children (5 female) with burosumab. All our patients had severe XLH. Mean age at initiation of burosumab therapy was 4.2±3.5 years. Mean serum phosphate was 0.69±0.18 mmol/L in males and 0.86±0.22 mmol/L in females (p=0.108). Mean ratio of tubular maximum reabsorption rate of phosphate to glomerular filtration rate (TmP/GFR)[1] was 0.55±0.11 mmol/L in males, and 0.76±0.23 mmol/L in females (p=0.06). The mean starting dose was 0.83±0.19 mg/kg subcutaneously every 14 days (males 0.79±0.19 mg/kg, females 0.87±0.21 mg/kg, n.s.). Two weeks after starting burosumab, serum phosphate was significantly different between males (0.90±0.21 mmol/L) and females (1.27±0.25 mmol/L, p=0.018). All males required a dose increase to try to normalize serum phosphate. On day 140 after starting, average dose in males increased further to 1.24±0.41 mg/kg to achieve a phosphate of 0.87±0.11 mmol/L while females had a normal phosphate and alkaline phosphatase on the starting dose. In male participants, at last follow up after a mean of 458±days, mean burosumab dose/kg was 1.68±0.61 mg/kg in males, the mean serum phosphate was 1.08±0.23, mean TmP/GFR was 1.01±0.20, the mean alkaline Phosphatase had normalized to 303.6±40.7 U/L, and mean $1,25(OH)_2$ vitamin D level was 186.4±16.6 nmol/L.

Conclusions: Our findings may suggest a sex difference in response to burosumab of XLH patients. Our data suggest that males may require a higher starting dose, possibly 1.2 mg/kg every 2 weeks.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-045 - Persistent benign proteinuria associated with CUBN variants

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Causes of persistent proteinuria are diverse, usually indicating a disease of the urinary system. If left untreated, proteinuria may contribute to kidney damage through various mechanisms including oxidative stress and inflammation. Therefore, persistent proteinuria mandates investigation and intervention. In asymptomatic children, at first orthostatic proteinuria or tubular proteinuria is suspected. Upon excluding these, a kidney biopsy is considered to rule out glomerulopathy. However, sometimes histology turns out to be non-specific. The recent discovery of *CUBN*, encoding the membrane glycoprotein cubilin, sheds light on some of those cases. Since cubilin is a component of the cubilin-amnionless-megalin complex that is responsible for the receptor-mediated endocytosis of albumin in the proximal tubules, a defect of cubilin leads to a reduction in albumin reuptake, consequently results in albumin-dominant proteinuria. Interestingly, variants located at the N-terminal of *CUBN* result in severe proteinuria and megaloblastic anemia, whereas variants at the C-terminal are associated with benign, isolated proteinuria.

Here we present five cases (M;F 3;2) with persistent proteinuria associated with homozygous or compound heterozygous C-terminal variants of *CUBN*. All patients presented with incidentally found isolated asymptomatic proteinuria, at their median age of 7 years (range 1.5 ~ 9). Their urine protein creatinine ratios were median 0.84 (0.57 ~ 2.03) mg/mg at presentation and did not change significantly over time regardless of RAS inhibition (median follow-up duration of 4 years [1 yrs~12yrs]). Their laboratory findings were also unremarkable at presentation or during follow-up for estimated GFR, serum albumin, lipid, hemoglobin, urine b2-microglobulin. None had hypertension, and kidney ultrasound showed normal kidneys. Among two patients, a kidney biopsy was done, which revealed no remarkable findings.
These cases are similar to previously reported cases, indicating benign proteinuria associated with C-terminal variants of *CUBN* needs to be considered in such cases.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-046 - Exome sequencing in a large cohort of individuals with VATER/VACTERL association for identification of disease-causing variants in disease-associated genes and prioritization of candidate genes

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Background: The acronym VATER/VACTERL association refers to the non-random co-occurrence of the following component features (CFs): vertebral defects (V), anorectal malformations (ARM) (A), cardiac defects (C), tracheoesophageal fistula with or without esophageal atresia (TE), renal malformations (R), and limb defects (L). The clinical diagnosis requires the presence of at least three CFs. Individuals presenting with two CFs have been termed VATER/VACTERL-like. As of now, only limited data concerning monogenic causes are available. By applying comprehensive genetic testing with parent-proband (trio) exome sequencing (ES) in a large cohort, the aim of this study was to extend the spectrum of disease-associated genes and to determine the diagnostic yield of monogenic disorders in VATER/VACTERL association.

Methods: Trio ES was performed in 88 individuals with VATER/VACTERL or VATER/VACTERL-like phenotype and their healthy parents.

Results: In 3/88 (3%) individuals, heterozygous disease-causing (pathogenic or likely pathogenic) *de-novo* variants in known

disease-associated genes/loci were identified: two individuals each harboring a pathogenic *KMT2D* variant associated with Kabuki syndrome and one individual with a pathogenic 8 Mb deletion on chr7p15.3-p21.2 encompassing *TWIST1* associated with syndromic craniosynostosis, among others. In the remaining 85 individuals (97%), no disease-causing variants in disease associated-genes could be found. Several genes were prioritized as candidate genes for VATER/VACTERL.
Conclusion: To our knowledge, this study encompasses the largest cohort of individuals with VATER/VACTERL analyzed by ES. Although ES is a comprehensive diagnostic tool for hereditary disorders, monogenic causes can only be identified in a small number of individuals with VATER/VACTERL association. This implies that monogenic disorders are not the predominant cause of VATER/VACTERL association and other pathomechanisms may exist. Rare variants in non-coding regions, polygenic inheritance or epigenetic factors may play a role in disease development. Nevertheless, the up to now prioritized candidate genes have to be further examined.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-047 - Novel management of hypophosphatemic rickets with hypercalciuria (HHRH)

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Background: Hereditary Hypophosphatemic Rickets with Hypercalciuria (HHRH) (*SLC34A3* gene, OMIM 241530) is an autosomal recessive disorder that results in a loss of function of the sodium-phosphate NPT2c channel at the proximal tubule. Phosphate supplementation rarely improves serum phosphate, hypercalciuria, nephrocalcinosis, 1,25$(OH)_2$ vitamin D (1,25$(OH)_2$D) levels or short stature.
Methods: We describe ^{23}Na MRI and the successful use of recombinant human growth hormone (rhGH) and Fluconazole to improve growth and hypercalciuria in a now 12-year-old male with HHRH (novel homozygous *SLC34A3* mutation, c.835_846+10del.T).
Results: The patient had chronic bone pain, hypophosphatemia (0.65mmol/L[reference interval 1.1-1.9]), pathological fractures and medullary nephrocalcinosis/hypercalciuria (urinary calcium/creatinine ratio 1.66mol/mmol[<0.6]). TmP/GFR was 0.65mmol/L[0.97-1.64]; 1,25$(OH)_2$D was >480pmol/L[60-208]. Rickets Severity Score was 4. Treatment with 65 mg/kg/day of sodium phosphate and potassium citrate 10 mmol TID failed to correct the abnormalities.
Adding rhGH at 0.35 mg/kg/week to the phosphate therapy, improved bone pain, height z-score from -2.09 to -1.42 over 6 months, without a sustained effect on TmP/GFR. Fluconazole was titrated to 100 mg once daily, resulting for the first time in a reduction of the 1,25$(OH)_2$D to 462 and 426 pmol/L; serum phosphate 0.87 mmol/L, and calcium/creatinine ratio of 0.73.
^{23}Na MRI showed normal skin (z-score +0.68) and triceps surae muscle (z-score +1.5) Na^+ levels; despite a defect in a sodium transporter, hence the patient was put on a low sodium diet.
Conclusions: The addition of rhGH, Fluconazole and salt restriction to phosphate/potassium supplementation improved the conventional therapy. Larger studies are needed to confirm our findings.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-048 - A case of genetic Steroid- Resistant Nephrotic Syndrome: Is it a new mutation for Schimke immune-osseous dysplasia?

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A case of genetic Steroid- Resistant Nephrotic Syndrome: Is it a new mutation for Schimke immune-osseous dysplasia?

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An eight years-old boy admitted to the hospital having generalized edema and severe proteinuria was diagnosed with nephrotic syndrome. His parents were cousins. In the physical exams we noticed he had short stature and showed pigeon chest skeletal deformity. His kidney ultrasound reports showed horseshoe kidney, decreased corticomedullary differentiation and mild hydronephrosis. He was resistant to steroid treatment, therefore we performed renal biopsy which further showed focal segmental glomerulosclerosis (FSGS). Treatment with cyclosporine was initiated. Whole exome sequencing test showed homozygous missense variant in SMARCAL 1 gene, exon 11, variant c.1754C>T p.S585F as likely pathogenic. PCR- Sanger sequencing was done. Unfortunately he became ESKD after 3 months and was resistant to all treatments. He underwent hemodialysis and is a candidate for kidney transplantation.
Conclusion: patients with steroid resistant nephrotic syndrome should be investigated for genetic disorders especially when the parents are relatives.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-049 - First interim analysis of the International X-Linked Hypophosphatemia (XLH) Registry: Pediatric baseline demographic and incidence of nephrocalcinosis and nephrolithiasis

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Objectives: X-linked hypophosphatemia (XLH) is a rare, progressive, hereditary phosphate-wasting disorder characterized by excessive activity of fibroblast growth factor 23. The International XLH Registry (NCT03193476) (initiated in August 2017, target enrolment:

1,200 children and adults with XLH, running for 10 years) will provide information on the natural history of XLH and impact of treatment on patient outcomes. These data are from the first interim analysis conducted on baseline data from pediatric subjects (age <18y).
Methods: At the time of analysis (Last Patient In: 30/11/2020; Database Lock: 29/03/2021), subjects diagnosed with XLH were enrolled from 81 hospital sites in 16 countries. Baseline parameters included demographics, medical and treatment history, and clinical presentation data.
Results: Overall, 360 children were included in this analysis; 61.7% female. Mean (SD) age 9.5y (±4.5). Treatment at entry was recorded for 281 subjects: 58.7% receiving burosumab (165/281); 40.6% conventional therapy (oral phosphate and active vitamin D) (114/281); 0.7% no treatment (2/281). Retrospective XLH clinical data were available at study entry for 239 children; nephrocalcinosis was noted in 23.8% (57/239). Two patients showed both nephrocalcinosis and nephrolithiasis. The frequencies of nephrocalcinosis in the different age groups were: 1–<5yrs (5/37; 13.5%), 5–<12yrs (30/118; 25.4%), and 12–<18yrs (22/84; 26.2%); and by treatment group at baseline: Conventional therapy (15/81; 18.5%), burosumab (39/115; 33.9%), no renal complications were recorded for the 2 untreated patients; it must be noted that this does not consider previous treatments and no causality between treatments and renal complications is implied.
Conclusions: This is the largest data set of children with XLH. Nephrocalcinosis is a frequent problem encountered in children with XLH. Renal complications and treatment information collected during the 10-year registry duration will generate real-world evidence to help inform clinical practice.
Authors acknowledge the contribution of all International XLH Registry Steering Committee members.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-050 - Nedosiran in primary hyperoxaluria subtype 1: interim results from an open-label extension trial (PHYOX3)

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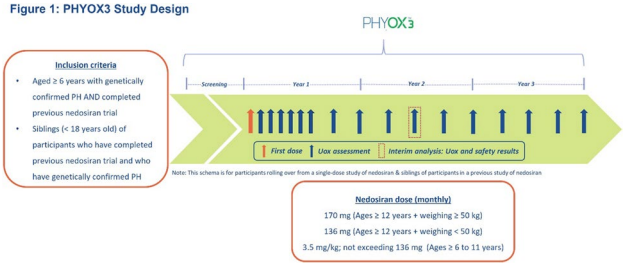
Background: Primary hyperoxaluria (PH) is a family of 3 (PH1, PH2, PH3) ultra-rare genetic disorders characterized by oxalate overproduction leading to renal formation of calcium oxalate stones, which may result in kidney failure. Nedosiran is an investigational RNA interference (RNAi) therapy in development for PH; it works by silencing hepatic lactate dehydrogenase enzyme expression (encoded by the *LDHA* gene). In a 6-month placebo-controlled pivotal trial, monthly subcutaneous (SC) nedosiran resulted in a significant and clinically meaningful reduction in urinary oxalate (Uox) excretion in participants with PH1.
Methods: PHYOX3 (NCT04042402) is a 3-year, open-label extension trial evaluating long-term safety and efficacy of monthly nedosiran in patients with genetically confirmed PH (Figure 1). An interim analysis of 13 PH1 participants who rolled over from the single-dose trial (PHYOX1) is reported here. After a single dose of nedosiran (1.5 mg/kg, 3 mg/kg, or 6 mg/kg), participants were monitored to allow their 24-hour Uox to return to baseline (drug washout).
Results: The drug washout period between nedosiran administration in PHYOX1 and re-treatment in PHYOX3 for the 13 participants with PH1 ranged from 10 to 23 months. After re-treatment with monthly nedosiran in PHYOX3, Uox once again fell robustly (mean maximum reduction > 80%) and this effect was sustained for at least 18 months. All participants achieved either normalization (85%; < 0.46/mmol/24-hr) or near-normalization (15%; ≥ 0.46 to < 0.6 mmol/24-hr) of Uox on at least one visit after Day 90 of resuming nedosiran. There were no drug-related serious adverse events and no premature discontinuations.
Conclusion: Nedosiran continues to show an acceptable safety profile. The persistent lowering of Uox over nearly 2 years of follow-up on monthly nedosiran suggests a durable clinical benefit in PH1.

Figure 1: PHYOX3 Study Design



Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-051 - Investigation of the Pathogenicity of a Novel Missense Variant in the ARHGAP24 gene by Quantitative Analysis of the Active Rac1 Protein: A Case of Pediatric Steroid-Resistant Nephrotic Syndrome

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Background: Steroid resistant nephrotic syndrome (SRNS) can lead to renal dysfunction, and one of its causative genes is *ARHGAP24* (NM_001025616.2). This gene encodes a Rho-GTPase

activating protein and acts as a negative regulator for Rac1 which is a small G protein. Excessive activation of Rac1 in podocytes has been reported to cause foot process effacement and lead to proteinuria and SRNS.
Case: The patient is a 15-year-old girl. She developed SRNS at the age of five. Although some immunosuppressive therapy including cyclosporine A (CyA) had been administrated, it was ineffective and severe proteinuria and hypoalbuminemia had continued. At the age of ten, a renal biopsy was performed and the pathological diagnosis was focal segmental glomerulosclerosis with CyA-induced tubulointerstitial damage. Therefore, CyA had been tapered off, and rituximab therapy was initiated. Subsequently, incomplete remission was achieved but her renal function gradually declined to Cre-eGFR 60 ml/min/1.73 m^2. Then we performed a comprehensive genetic analysis of podocyte-related genes by targeted next-generation sequencing using peripheral blood samples from the patient and her parents. A novel missense variant (c.1217G>T, p.(Ser406Ile)) in the *ARHGAP24* gene was detected, and it was a *de novo* variant. In addition, the quantitative analysis of active Rac1 in HEK293T cells transfected with the *ARHGAP24* plasmid vector carrying the variant was performed, and a significant increase of active Rac1 was observed compared to the wild type. Then, we diagnosed this case as SRNS associated with the *ARHGAP24* gene variant.
Discussion: It is definitely important to determine whether a novel variant is pathogenic or not because almost immunosuppressive therapy for SRNS associated with genetic variants is often ineffective. In patients with *ARHGAP24* variants, quantitative analysis of active Rac1 protein is a relatively simple and universal test for its pathogenicity. This analyzing method is considered to be useful in determining pathogenicity.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-052 - The role of podocytes in cystinosis disease: a new possible therapeutic strategy?

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Background: Cystinosis is a rare, incurable autosomal recessive storage kidney disease caused by mutations in CTNS gene, which encodes the cystine transporter cystinosin and leads to lysosomal cystine accumulation in all the body. In addition to proximal tubular cells, cystinosis also affects the glomerulus since podocytes are lost into urine leading to proteinuria and kidney failure. Cysteamine, the current treatment, decrease cystine accumulation but does not reverse proximal tubular injury (renal Fanconi syndrome) neither glomerular injury. These evidences suggest that different mechanisms are involved and further studies are necessary to understand the disease in order to develop new therapeutic options.
Methods: Immortalized patient-derived cystinosis and healthy podocytes were used and the results were validated in our in-house developed cystinosis zebrafish model. To study the altered metabolic pathways, metabolomic analysis (LC-MS), flow cytometry, RT-qPCR, western blot, chemical and redox-sensing fluorescent probes were used.
Results: Cystinosis podocytes present a peculiar cellular metabolism, characterized by impaired glycolytic and TCA cycle, increased ROS levels and cell detachment. Interestingly, treatment with targeted compounds improved the impaired phenotype both in vitro and in vivo.
Conclusions: An impaired podocyte metabolism is a critical feature in cystinosis and it elucidates the importance to investigate more targeted therapies in combination with the standard of care cysteamine.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-055 - Confusing C3 dominant deposit in WT1 nephropathy : A rare case

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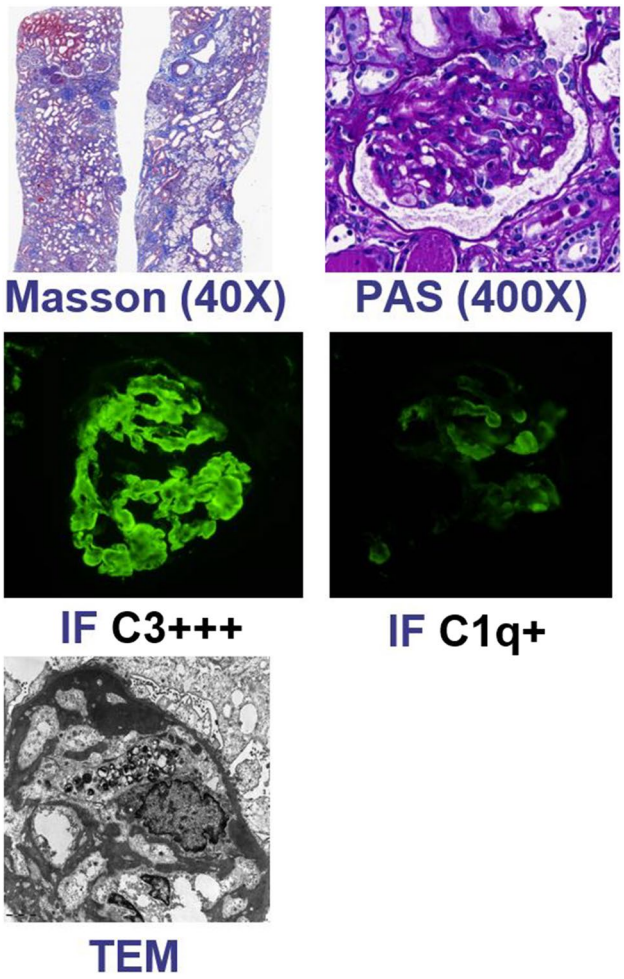
Backgrounds: Glomerular lesions in *WT1* disorder are variable, while diffuse mesangial sclerosis (DMS) in Denys-Drash syndrome (DDS) and focal segmental glomerular sclerosis (FSGS) in Frasier syndrome (FS) comprise the major part. MPGN was occasionally seen in *WT1* nephropathy, but C3 dominant deposit had been rarely reported.
Case: A 10-year-old girl was referred with a complaint of anasarca for 5 days. Examination at local hospitals revealed proteinuria, renal insufficiency (BUN of 9.4mmol/L, SCr of 209.5umol/L), hypoalbuminemia (12.3g/L), hypercholesterolemia (15.87mmol/L) and hypocomplementemia (0.45g/L). No related family history was noted. PE reveal hypertension, short stature, anasarca, and tonsil enlargement at one degree. Deeper laboratory findings included anemia (Hemoglobin 108g/L), hypoalbuminemia (14g/L), hypercholesterolemia (16mmol/L); Elevated PCT (0.16ng/mL), proteinuria (5.53g), ASO (320 Ku/L), anti-DNase-B (1440U/mL,) and iPTH (181pg/mL); decreased C3 (0.71g/L) and eGFR (30mL/min/1.73m^2). Examinations for secondary NS were negative. Ultrasound showed normal-size kidneys with hyperechogenicity. Chest CT revealed bilateral pleural effusion with segmental atelectasis. Edema gradually resolved after diuresis. She developed bronchopneumonia 5 days after admission, which relieved after intravenous piperacillin/tazobactam. Renal biopsy revealed MPGN with intensely C3 deposition (Diffuse and glomerular C3+++ and C1q+ in clumps; Exudative mild IgG and IgM). C3 glomerulopathy was suspected. TEM revealed dense deposition in subendothelial and mesangial area, with occasional subepithelial deposition. Examination for alternative complement pathway was delayed due to financial reasons. Methylprednisolone pulses followed by oral prednisone and intravenous cyclophosphamide were given. After a few weeks, genetic testing revealed no complement system-related gene disorder, but a variant in *WT1* (c.1447+4C>T, intron 9) which has been reported repeatedly. Karyotype analysis were normal. Immunosuppressive therapy was then stopped, without effectiveness.
Conclusions: Atypical presentations of renal pathology in genetic disorder makes diagnosis more confusing. Susceptibility due to congenital disorder, and concomitant infection, may be reason of the atypical deposit in the case.

Fig. 01 Renal pathology (LM, IF and EM)



Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-056 - Proteinuria and renal insufficiency of Branchio-oto-renal syndrome with EYA1 variants: Case series

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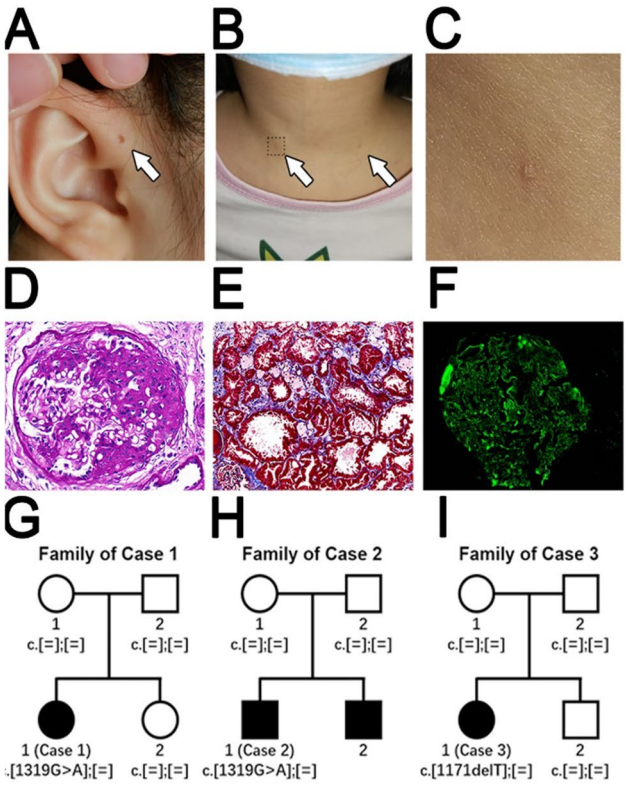
Backgrounds: Branchio-oto-renal syndrome (BOR) is a genetic disorder characterized by hearing loss, preauricular pits, branchial anomalies, and renal anomalies. Knowledge of renal involvement was concentrated in structural abnormalities. However, some patients presented as "glomerular diseases", misleading in diagnosis.
Case: Case 1 was a 9-year-old female with proteinuria and increased SCr detected for 1 year. WES at local hospital revealed no pathologic variants. Renal biopsy revealed "MsPGN". Glucocorticoid and MMF were given, but ineffective after 1 year. During physical examination at admission, unexpected preauricular fistulas and anterior cervical fistulas were noted. Examination revealed eGFR of 36mL/min/1.73m2 and proteinuria of 39.0~68.9 mg/kg/d. Mild hearing loss was found. Renal pathology was reassessed: Segmental glomerular sclerosis, proliferation of mesangial cells, and multifocal tubular atrophy with foam cells; IgG+, IgM+, C3+ and C1q+; Dense deposition in subendothelial, mesangial area and GBM. Trio-WES was reperformed, revealing a pathogenic variant (c.1319G>A) of *EYA1*. Immunosuppressive therapy was withdrawn. eGFR and proteinuria remained stable after 6 months. Case 2 was an 8-year-old boy with increased creatine for 3 years. In childhood, he had been found preauricular fistula, conductive deafness and renal insufficiency. Genetic examination was refused then. At admission, BOR was clinically diagnosed by typical presentations. Trio-WES revealed pathogenic variant (c.1319G>A) of *EYA1*. Transplant was being waited. Case 3 was an 8-year-old girl with complaints of increased creatinine detected for 10 days. She had a pit at mandibular angle and preauricular pits. Examination revealed proteinuria of 0.553~0.758 g/d and ESRD. Hearing impairment was found. Trio-WES revealed a pathologic variant (c.1171delT) of *EYA1*, without previous report. Allograft renal transplantation was performed. Follow-up at 1 year revealed normal renal function.
Conclusion: Awareness of BOR and detailed physical examination are important for early diagnosis of this multi-system disorder. Immunosuppressive therapy seems not effective in proteinuria with immune complex deposits in BOR patients.



A to C: Physical examination of case 1.
D to F: Pathology of renal biopsy of case 1.
G to I: Pedigrees of case 1, 2 and 3.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-057 - X-linked hypophosphatemic rickets (XLH). Report of first patient treated with Burosumab in Mexico

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1-year-old female, clinically with Genu Varu deformity, difficulty walking, and hypophosphatemia, mother with X-linked hypophosphatemic rickets (XLH), laboratory studies: Urea 28.4 mg/dl, Creatinine 0.43 mg/dl, Calcium 9.85 mg/dl, Phosphorus 2.9 mg/dl . Alkaline phosphatase 462.3 U/L, Percentage of phosphorus reabsorption 60%. PHEX variant c2071-2>G pathogenic heterozygous variant. Treated with phosphate and calcitriol solution at conventional doses for 23 months. She persisted with the Genu Varo deformity, difficulty walking, and hyphosphatemia: Urea 21.9 mg/dl, Creatinine 0.5 mg/dl, Calcium 9.5 mg/dl, Phosphorus 2.8 mg/dl, Alkaline phosphatase 371.1 U/L. Conventional treatment is suspended for 2 weeks "washout phase" to start treatment with Burosumab 8 mg/kg/dose. The cohort at 40 weeks of treatment with Burosumab reports: Urea 30.6 mg/dl, Creatinine 0.4 mg/dl, Calcium 9.9 mg/dl, Phosphorus 3.4 mg/dl, Alkaline Phosphatase 273.4 U/L, Genu Varo reduction and improvement in the ability to walk.
XLH is a mineral homeostasis disease characterized by renal loss of phosphate with multisystem involvement caused by a mutation in the PHEX gene, causing the osteocyte to produce excessive amounts of FGF-23; it increases the urinary excretion of phosphate, and decreases the action of 1-α hydroxylase and the concentration of 1,25(OH)2D, reducing intestinal absorption of phosphorus, causing hypophosphatemia.
Burosumab is a monoclonal antibody against FGF-23 that restores phosphorus homeostasis, normalizing its serum values through improved renal phosphorus reabsorption and increased production of 1,25(OH)2D. This results in improvement of the skeleton, in the severity of rickets, in the bowing of the legs and in the ability to walk and play sports.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-058 - X-linked hypophosphatemia: not only a skeletal disease but also a chronic inflammatory state

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X-linked hypophosphatemia (XLH) is a rare genetic disease caused by a primary excess of FGF23. FGF23 has been associated with inflammation and impaired osteoclastogenesis, but these pathways have not been investigated in XLH. The aim was to evaluate whether XLH patients display peculiar inflammatory and osteoclastic profile. We performed a prospective multicenter cross-sectional study analyzing transcript expression of 8 inflammatory markers (Il6, Il8, Il1β, CXCL1, CCL2, CXCR3, Il1R, Il6R) by RT-qPCR on PBMCs extracted from total blood samples. In total, 28 XLH patients were enrolled, 11 adults and 17 pediatrics patients (composed of one subgroup of 6 SOC (standard of care) treated patients and the second of 11 burosumab treated patients); plus 19 healthy controls. The expression of all inflammatory markers (except Il6R) was significantly increased in PBMCs from XLH patients as compared to controls. No differences were observed between the two sub-groups of patients. In addition, the effect of native /active Vitamin D on XLH patient osteoclast formation was assessed by quantification of multinucleated TRAP positive osteoclasts generated in vitro from XLH patient's PBMCs versus healthy controls. Osteoclast formation was significantly impaired in XLH patients when compared to controls, however those derived from burosumab treated patients showed a restored response to native vitamin D. XLH mature osteoclasts displayed higher level of inflammatory markers. The inflammatory profile at the end of the osteoclastic differentiation process was lower in cells derived from patients receiving burosumab compared to the one derived from SOC's sub-group. We describe for the first time a peculiar inflammatory profile in XLH. Since XLH patients have a propensity to develop arterial hypertension, obesity and enthesopathies, and inflammation can worsen these clinical outcomes, we hypothesize that inflammation plays a crucial role in these extra-skeletal complications of XLH.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-059 - European multicenter experience with RNA interference medication (Oxlumo®) in patients with Primary Hyperoxaluria type 1

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Primary hyperoxaluria type 1 (PH1) is a rare metabolic disorder of the glyoxylate metabolism inducing endogenous oxalate overproduction. A first RNA interference (RNAi) medication now available, Oxlumo® (Alnylam Pharmaceuticals, USA) targeting the mRNA of glycolate oxidase, reduces oxalate, but increases glycolate production. We report 25 PH1 patients (10 female, age 1-62 years): 7 on hemodialysis, one on peritoneal dialysis and 17 on stable kidney function (eGFR > 30 and < 55 ml/min in 2 and > 70 in all others) treated with Oxlumo®. Plasma oxalate (Pox) and glycolate (Pglyc) were determined before every dosage, as was urinary oxalate (Uox) and glycolate (Uglyc) excretion in patients with stable kidney function. Three tesla bone MRI was performed before dosing and 6 monthly in 4 dialysis

patients. Data of 15 (5 on dialysis) patients with at least four dosages were evaluated. Uox was normal (< 0.5 mmol/1.73m^2/d) in 2, near normal (< 0.75) in 5 and above 0.75 in 3 patients. Pox was normal in 7 (< 7.4 µmol/l) and elevated in 3 patients. Data post 5th to 7th dosage was available in 5 patients, Uox, was normal in one, but >0.75 in all other. In dialysis, Pox did not decline (median 45.1 at baseline, n = 7; and 39.9 post 4th dosage, n = 5), as was Pglyc (86.05 vs 71.1). PGlyc remained stable (under B6), but increased >1 mmol/l inducing lactic acidosis (without B6) in one patient. Bone MRI remained unchanged after 6 or 9 months in patients evaluated.
Oxlumo® is capable of significantly reducing Uox in monthly dosing, however, adjustment of dosage may be necessary for quarterly dosing. In dialysis, lack of Pox reduction maybe related to dissolving systemic oxalate deposits, but bone MRI did not show improvement yet. PGlyc needs more careful control in dialysis patients.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-060 - Relationship of baseline weight and response to lumasiran in patients with primary hyperoxaluria type 1 on hemodialysis

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Background: Primary hyperoxaluria type 1 (PH1) is a rare genetic disorder characterized by oxalate overproduction that can lead to end-stage kidney disease. We report the relationship between baseline weight and response to lumasiran, an RNA interference therapeutic that inhibits oxalate production, using data from ILLUMINATE-C (NCT04152200) patients on hemodialysis at enrollment.
Methods: Patients on hemodialysis with genetically confirmed PH1 and a predialysis plasma oxalate (POx) value ≥20 µmol/L were enrolled into Cohort B of ILLUMINATE-C. In this post hoc analysis, Cohort B patients were stratified by weight (<10, 10 to <20, ≥20 kg), with each weight category corresponding to a different dosing regimen. Change from baseline in POx and plasma glycolate were analyzed after 6 months of lumasiran treatment.
Results: Fifteen patients were enrolled in Cohort B (median age 6 [range, 1–59] years **[Table]**). Median (range) time from diagnosis to first dose was 1.4 (0.5–36.7) years. Numbers of dialysis sessions per week, genotypes, and pyridoxine use prior to enrollment were similar across subgroups at baseline. Lower-weight subgroups had higher baseline median predialysis POx values (**Table**). The least-squares mean reductions from baseline in POx at Month 6 (average of Month 3 to Month 6) were comparable across subgroups (41.3%–44.4%). Plasma glycolate initially increased and then plateaued across subgroups. Treatment-related adverse events were comparable across subgroups; none were serious or severe. No treatment-emergent anti-drug antibodies were observed.
Conclusions: Patients treated with lumasiran experienced consistent reduction in POx levels, irrespective of weight category. While lower-weight subgroups had higher baseline median predialysis POx values, the least-squares mean reductions in POx at Month 6 were comparable across subgroups.

ILLUMINATE-C: Patients on Hemodialysis at Enrollment	Baseline Weight (kg) <10 (N=5)	10 to <20 (N=3)	≥20 (N=7)	Overall Cohort B (N=15)
Select baseline demographic and clinical characteristics				
Age at consent, median (range), years	1.2 (1–3)	6.0 (2–6)	18.0 (16–59)	6.0 (1–59)
Time from diagnosis to first dose, median (range), years	1.0 (0.5–3.3)	0.8 (0.5–6.0)	1.6 (0.6–36.7)	1.4 (0.5–36.7)
Genotype,[a] n (%)				
PR/*	1 (20)	1 (33)	3 (43)	5 (33)
M/M or M/N	2 (40)	1 (33)	4 (57)	7 (47)
N/N	2 (40)	1 (33)	0	3 (20)
Pyridoxine use, n (%)	2 (40)	1 (33)	4 (57)	7 (47)
Predialysis POx, median (range), µmol/L	122.3 (93.1–152.3)	119.0 (106.3–122.5)	97.1 (56.3–167.0)	103.7 (56.3–167.0)
Plasma glycolate, median (range), µmol/L	273.5 (249.0–487.0)	499.5 (366.5–655.0)	178.0 (73.9–563.5)	273.5 (73.9–655.0)
Number of dialysis therapy sessions per week, median (range)	6.0 (3–7)	6.0 (5–6)	5.0 (3–6)	6.0 (3–7)
Pharmacodynamic endpoint				
Percent change in POx from baseline to Month 6[b], LS mean (SEM)[c]	-42.8 (8.4)	-44.4 (2.8)	-41.3 (7.3)	-42.4 (4.0)

[a]M=missense; N=nonsense; PR=pyridoxine-responsive; *=any genotype of PR, M, or N. PR was defined as NM_000030.3 (AGXT):c.508G>A (p.Gly170Arg) or NM_000030.3 (AGXT):c.454T>A (p.Phe152Ile). [b]Average of Month 3 through Month 6. [c]Mixed model for repeated measures was used.
Abbreviations: LS, least-squares; POx, plasma oxalate; SEM, standard error of the mean.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-063 - 30-year Outcome of Primary Hyperoxaluria type 1

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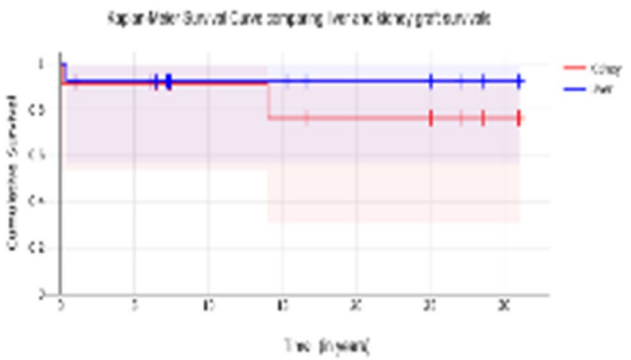
Primary hyperoxaluria type 1 (HP1) can present as oxalate stones, nephrocalcinosis and/or kidney failure. Treatment options consist in nychthemeral hyperhydration, crystallization inhibitors, pyridoxine, RNA interference therapy and liver-kidney transplantation. This retrospective study aims to describe the long-term outcome of children with HP1 over the last 30 years.
The 28 consecutive children diagnosed with PH1 between 1990-2020 at our center were included.
Mean follow-up was 16.7 years (2.5-41.2) with mean age at last follow-up being 20.3 years (3-41.5). 13/28 were on conservative management at a mean age of 4.4 years (0.5-16) (hyperhydration and pyridoxine). Nine of them participated to randomised-controlled

trials investigating novel drugs (lumasiran, stiripentol, oxabacter). 5/5 patients showed complete response to lumasiran after an average 6th dose (9-12 months) demonstrated by urinary oxalate excretion being within normal limits. Data on stiripentol response are pending. Fifteen children reached kidney failure at a mean age of 2.7 years (0.1-12) and received combined liver-kidney (11), or sequential liver-kidney transplants (2), or remained on dialysis (2). One child each underwent a second and third kidney transplantation. One child succumbed between the liver and kidney sequential transplantations. Mean pre-transplant dialysis was 29 months (4-86). No patient required postoperative hemodialysis . Maximal diuresis was induced post-transplant with intravenous and intragastric hyperhydration (>3 L/m^2/day). No disease recurrence was observed after transplantation. 10-year and 20-year liver graft survivals were 92%, and kidney graft survival was 91.7% and 76.3%, respectively. Mean creatinine clearance among transplanted and non-transplanted groups were 91.6 ml/min/1.73 m^2 (55-105); and 111 ml/min/1.73 m^2 (79-141), respectively. About half of the patients in this series have normal kidney function with conservative treatment. The others are doing well with a functioning graft except for one who died following liver transplantation. The novel specific treatments are expected to further improve the prognosis of this rare and severe disease.



Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-064 - Clinical and molecular characteristics of children with primary hyperoxaluria type 1

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Introduction: Primary hyperoxaluria type 1 (PH1) (MIM #259900) is a rare autosomal recessive disease characterized by hyperproduction of oxalates in liver due to pathogenic variants in *AGXT* gene leading to nephrocalcinosis (NC) and/or urolithiasis (UL) and CKD. The aim of the study was to investigate clinical and molecular characteristics and kidney outcomes in children with PH1.
Methods: Retrospective analysis of phenotype and genotype of ten children (6M/4F) with genetically confirmed PH1 was conducted. The median follow-up was 2.5 (IQR: 1.3; 5.9) years.
Results: The first clinical signs of PH1 were found in 7 (70%) of children before the age of 1 year and in 3 (30%) patients between 1 and 5 years. At presentation NC was revealed in 6 (60%) children, NC and UL in 3 (30%) and UL in 1 (10%) case. The age of genetic diagnosis of PH1 was significantly later compared to the age of manifestation of the disease: 30.0 (8.0; 54.0) and 3.0 (1.0; 18.5) months (p=0.004). *AGXT* variant c.508G>A (p.Gly170Arg) was identified in 6 (60%) children (homozygous (n=2), compound heterozygous (n=4)). There were 4 B6-responsive patients (homozygous (n=2), compound heterozygous (n=2)). At the last follow-up CKD2 had 4 (40%), CKD3 - 4 (40%), CKD5 - 2 (20%) patients. Transplantation (Tx) was performed in 2 children: combined sequential liver and kidney Tx in 1 child with compound heterozygous *AGXT* variant (c.166-1G>C; c.508G>A) and preemptive liver Tx in 1 kid with compound heterozygous *AGXT* variant (c.32_33delCC; c.508G>A). One teenager with homozygous *AGXT* variant c.364C>T (p.Arg122Ter) died due to complications of systemic oxalosis.
Conclusion: All patients with PH1 presented with NC/UL. Infantile form of PH1 was observed in 70% of children. Despite the B6-responsitivity found in 40% of patients with *AGXT* variant c.508G>A all children had CKD2-5. Effective treatment is needed to prevent progression of PH1 to CKD.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-065 - Examination of disease onset mechanism due to OCRL gene splicing abnormality

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Background: Mutations in *OCRL* gene are associated with both Lowe syndrome and Dent disease-2, and the genotype/phenotype correlation has been clarified. However, no studies have been conducted on mutations that cause abnormalities in splicing.
Method: We included 21 reported *OCRL* splicing variants from the Human Gene Mutation Database (HGMD) in which *OCRL* splicing abnormality was predicted by *in silico* analysis. We evaluate the consequences of the mutations in the mRNA level by minigene system.
Result: Abnormal splicing was detected in 20 of 21 cases, indicating that altered pre-mRNA splicing in *OCRL* gene might involve in the onset of diseases. In addition, various splicing patterns were shown, including exon skipping, inclusion of cryptic exon, the loss of an exon fragment and inclusion of an intron fragment.
Discussion: In this study, there were multiple cases which indicated the relation between splicing pattern and phenotype. This study provided important information not only in the pathogenesis mechanism of *OCRL* gene splicing abnormality but also the disease phenotype.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-066 - Clinical Utility of Genetic Testing in Indian Children with Kidney Diseases

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Background: Almost one-third of children with kidney diseases have a genetic aetiology with overlapping spectrum of manifestations. This retrospective study aimed to evaluate the clinical utility of genetic testing in the diagnosis and management of Indian children with suspected genetic kidney diseases.
Methods: Children below 18 years in whom a genetic test was ordered from September 2016 to January 2021 were included. Clinical indication for genetic testing was categorized as Glomerular diseases, tubular disorders, nephrolithiasis and/or nephrocalcinosis, cystic kidney diseases, congenital abnormality of kidney and urinary tract (CAKUT), chronic kidney disease of unknown aetiology and others. The genetic test of choice was exome sequencing. Variants were classified as per the American College of Medical Genetics guideline.
Results: One hundred thirty-one samples were sent for genetic testing from 121 index children, 8 parents and 2 foetuses. Ninety-nine variants were reported in 54 genes. Out of 99 variants, 54 were missense, 11 nonsense, 18 frameshifts, 1 indel, 10 splice site and 5 were copy number variants. Thirty-two children (26.4%) had pathogenic and 18 (14.8%) had likely pathogenic variants. Thirty-two children (26.4%) had variants of uncertain significance. No variants were reported in 39 children (32.2%). A genetic diagnosis was made in 50 children with an overall yield of 41.3%. The diagnostic yield was 29.6% (16/54) for glomerular diseases, 53.3% (8/15) for tubular disorders, 62.5% (10/16) for nephrolithiasis and/or nephrocalcinosis, 58.8% (10/17) for cystic kidney diseases, 66.6% (4/6) for chronic kidney disease of unknown aetiology and 20% (2/10) for CAKUT. Genetic testing made a new diagnosis or changed the diagnosis in 17 children (14%).
Conclusion: Almost 40% of children who underwent genetic testing had a genetic disease. Genetic testing confirmed the clinical diagnoses, made new diagnoses or changed the clinical diagnoses which helped in appropriate management.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-067 - The High Impact of Accessible Genetic Testing in an Underserved Pediatric Nephrology Cohort

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Background: Next generation sequencing (NGS) allows identification of genetic etiologies in a sizable portion of pediatric-onset renal disease patients. Historically, testing has been cost prohibitive which limits access to underserved pediatric populations.
Objective: To observe how incorporation of commercially available 385 gene panel for kidney disease impacts clinical diagnosis and management in an underserved pediatric nephrology cohort.
Design/Methods: Patients receiving care at St Christopher's Hospital, Philadelphia PA for kidney disease underwent genetic testing with the RenasightTM test. Positive findings were defined as a single pathogenic (P) or likely pathogenic (LP) variant for an X-linked or autosomal dominant condition, two P/LP variants for an autosomal recessive condition, and the presence of two *APOL1* high-risk alleles (G1 or G2). Other genetic findings that were not considered positives include carriers (one P/LP variant in an autosomal recessive condition) and variants of uncertain significance, which were reported for a subset of patients for whom it was requested.
Results: From Oct 2020 to Oct 2021, 194 patients were tested. The median patient age was 14 years. When reported, a high proportion of these individuals identified as African American and/or Hispanic **(Table 1)**. In addition, 68% of patients were covered by government-based public insurance **(Table 2)**. Positive findings were identified in 40% (77/194) of patients across 26 genes. The most common positive findings involved the *APOL1* and *PKD1* genes. Positive test results led to changes in medical management in 86% of cases.
Conclusions: Genetic testing identified a genetic basis for renal disease in 40% of patients. A large gene panel allows for broad evaluation of multiple genes associated with kidney disease that are otherwise difficult to distinguish clinically. This approach provides accessibility to information that can optimize medical management in underserved patient populations.

Table 1: Patient Demographics

	N	*Percentage*
Gender Counts		
Male	110	57%
Female	84	43%
Age Breakdown		
Age 0-<1 year	4	2%
Age 1-<11 years old	72	37%
Age 11-<18 years old	85	44%
Age 18-21 years old	16	8%
Age >21 years old	17	9%
Ethnicity counts		
African American/Black	35	18%
Hispanic/Latin American	35	18%
European	14	7%
Caucasian/Non-Hispanic White	8	4%
Asian	2	1%
Unknown	10	5%
Not Provided	84	43%
Other	6	3%

Table 2: Insurance Type

	N	*Percentage*
Insurance Type		
Commercial/Private Insurance	47	27%
Government Based Insurance	117	68%
Other/Unknown	9	5%

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-068 - Disease-causing variants in LMX1B associated with nail-patella syndrome and focal segmental glomerulosclerosis

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Background: Nail-patella syndrome (NPS) is a rare autosomal dominant inherited syndrome with a broad phenotypic spectrum comprising dysplasia of the nails, patellae, elbows and the presence of iliac horns. Up to 50% of the individuals show renal involvement ranging from hematuria and proteinuria to end stage kidney failure (ESKF). Focal segmental glomerulosclerosis (FSGS) is a rare histopathological pattern seen in these individuals. NPS is caused by heterozygous disease-causing variants in *LMX1B* encoding the LIM homeodomain transcription factor. Here we report on four families with different disease-causing variants detected by exome sequencing (ES) and the histological picture of FSGS in kidney biopsy.
Methods: In addition to a detailed phenotypic characterization of affected individuals, ES was performed in the index followed by targeted Sanger sequencing of available relatives.
Results: In a young Rumanian male and his father the heterozygous likely pathogenic variant p.(Trp266Arg) in *LMX1B* was identified. Both individuals presented with ESKF, thorax malformations, antebrachial skin pterygium, hypoplastic nails and completely missing patellae. In one German female with childhood onset proteinuria leading to kidney transplantation at the age of 29 years, dystrophic nails and a shortened fourth toe, the heterozygous pathogenic variant p.(Met306fs*50) was identified. In another German family, the heterozygous pathogenic variant p.(Arg246Gln) was detected in two individuals presenting with isolated nephropathy and subsequent ESKF. In a Turkish female presenting with microscopic hematuria and proteinuria since adolescence, the paternally inherited heterozygous pathogenic variant p.(Pro311Argfs*48) was identified. In three of the four families, kidney biopsy was performed and FSGS was seen histologically in all cases.
Conclusion: Despite its very small size, this study highlights that in individuals with isolated nephropathy and the histological pattern of FSGS, NPS should be considered as causative. Therefore, in individuals with FSGS and the possibility of a hereditary cause, molecular examination of *LMX1B* should also be initiated.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-069 - eGFR equations in young ADPKD patients: one or the other?

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Objectives: Young ADPKD could benefit from novel disease altering therapies. However, the lack of sensitive and validated endpoints in this population renders clinical trials very challenging. We aimed to evaluate methods for the estimated glomerular filtration rate (eGFR) to identify the most accurate method for this population.
Methods: Serum creatinine (SCr) and serum Cystatin C (SCysC) were measured in a large cohort of genotyped young ADPKD patients with long-term follow-up. Commonly used equations for eGFR were compared for their relative performance, using the reference intervals for healthy children and young adults.
Results: We included 68 genetically confirmed young ADPKD patients (sex ratio 1:1) with a mean age of 10.2 years (min-max: 0-23 years) and with a mean time of follow-up of 3.6 years (min-max: 1-8 years). SCr was mostly within the reference interval, regardless age and sex. The revised Schwartz formula (CKiD) showed a highly significant and clinically important decline in eGFR with aging (-3.31ml/min/1.73m^2/year, $p<0.0001$). The recently updated equation by the Schwartz group (CKiDU25) showed a smaller (-0.90 mL/min/1.73m²/year) but significant ($p=0.001$) decline in eGFR with aging and also showed a significant unexplainable sex difference ($p<0.0001$). SCr normalized for Q and the related FAS-SCr did not show a clear age or sex dependency (table 1). Finally, CysC based and combined equations were independent of age and sex in this ADPKD patient cohort.
Conclusion: The CKiD equation, the most widely used method to calculate eGFR in children, and the CKiDU25 were associated with unexpected age or sex differences in the young ADPKD population. In contrast, FAS-SCr, FAS-CysC and the combined FAS equation using normalized biomarkers showed no age and sex dependency and might therefore be more reliable to monitor kidney function in this population. This finding could help future design of the upcoming clinical trials.

Table 1. Comparison of the different eGFR equations and SCr & SCysC normalized by Q. A p-value of < 0.0023 was considered significant to account for multiple testing.

Equation	Gender effect mean value F/M (p-value)	Age effect (mL/min/1.73m²/year)	133.9 < Fr < 160.1 (mL/min/1.73m²)	Fr > 160.1 (mL/min/1.73m²)
CKiD	124.9 / 127.4 (NS)	-3.31 (p < 0.0001)	23.6%	12.0%
CKiDU25	110.0 / 124.7 (< 0.0001)	-0.90 (p = 0.0011)	14.6%	5.5%
FAS-Age	119.7 / 125.5 (p = NS)	-0.61 (p = NS)	17.5%	6.6%
FAS-Height	122.2 / 131.7 (p = 0.0020)	-0.98 (p = 0.0005)	20.4%	9.1%
EKFC	107.2 / 111.6 (p = 0.0008)	-0.27 (p = 0.0004)	1.1%	0.0%
LMR18	101.9 / 107.4 (p = 0.0002)	-0.45 (p = 0.0004)	0.4%	0.0%
CKD-EPI40	105.3 / 112.0 (p = 0.0001)	-0.08 (NS)	0.4%	0.0%
FAS-CysC	104.7 / 101.7 (NS)	0.096 (NS)	1.8%	0.4%
Fas-Combined	112.3 / 114.0 (NS)	-0.2872 (NS)	6.18%	1.09%
Equation	**Gender effect mean F/M (p-value)**	**Age effect (mg/dL/year)**	**Fr < 0.80 (mg/dL)**	**Fr < 0.67 (mg/dL)**
SCr/Q	0.93 / 0.88 (NS)	+0.0044 (NS)	17.1%	6.9%
Equation	**Gender effect mean F/M (p-value)**	**Age effect (mg/L/year)**	**Fr < 0.80 (mg/L)**	**Fr < 0.67 (mg/L)**
CysC/Q'	1.06 / 1.07 (NS)	-0.001 (NS)	1.8%	1.5%

F: female, M: male, Fr: fraction, NS: not statistically significant. Fractions with cut-off values (133.9-160.9 ml/min/1.73m²) were derived from the FAS-equation (107.3/[SCr/Q]). The lower and upper limit for SCr was 0.68 and 1.33 mg/dL, respectively. Symmetrically, 107.3 + (107.3-80.7)= 133.9. The fractions for SCr and SCysC normalized by Q were derived from the reference intervals 0.67-0.80mg/(d)L (107.3/0.67=160.1, 107.3/0.80=133.9).

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-070 - Clinical and diagnostic utility of genomic sequencing for children with microscopic haematuria in a Renal Genetics Clinic

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Background: Microscopic haematuria (MH) in children is associated with the risk of progression to chronic kidney disease. Genetic disease including Alport syndrome is an important potential aetiology.
Method: We conducted a retrospective review of the electronic medical records of patients referred to a Renal Genetics Clinic (RGC) with MH from 2016 to 2021. Data were collected including demographics, investigations and diagnosis prior to referral, tests undertaken by the clinic, and the diagnostic and clinical utility of these genetic tests.
Results: Sixty patients were referred to the RGC with MH over a six-year period. Mean age at referral was 8.8 years and most (73%) were referred for diagnosis of an undifferentiated disease. At time of review, 10 (17%) patients' genetic results were outstanding. 21 (35%) patients had analysis of a limited haematuria panel (COL4A1, COL4A3, COL4A4, COL4A5, MYH9) with 12 (57%) receiving a genetic diagnosis. 24 (40%) had further analysis and 9 (38%) received a diagnosis. 5 (8%) patients underwent cascade testing for a known familial variant and all received a diagnosis. 11 (18%) had a variant of uncertain significance (VUS) in a phenotypically concordant gene.
Degree of haematuria and presence of proteinuria was correlated with diagnostic yield; 63% of those with >500x10^6/L RBC and 58% of those with a urinary protein:creatinine ratio >20 received a genetic diagnosis.
Importantly, negative genetic analysis can still have significant clinical utility for patients by altering surveillance and further management; we found the genetic result had clinical utility in 62% of patients.
Conclusions: Our RGC review highlights the substantial clinical utility of genetic analysis for microscopic haematuria in paediatric patients. The testing is non-invasive and has a high diagnostic yield. A multidisciplinary team including appropriate genetic counselling can help ensure these patients are followed up meaningfully.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-071 - A case of hypoplastic kidneys, ocular coloboma and optic atrophy with de novo mutations in both PAX2 and OPA1 genes

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Introduction: Renal coloboma syndrome (RCS) characterized by kidney and eye abnormalities is mainly caused by heterozygous mutation of the *PAX2* gene which does not usually cause progressive blindness. Dominant optic atrophy caused by heterozygous mutation of the *OPA1* characterize irreversible bilateral blindness that almost always presents in young patients. We report a case of hypoplastic kidneys, ocular coloboma and optic atrophy with *de novo* mutations in both *PAX2* and *OPA1* genes.
Case report: Oligohydramnios was observed at 6th month of gestation in a patient. A female neonate was born at 38 weeks of gestation with a birthweight of 3064 g. She had bilateral nystagmus, and MRI at 4 months of age indicated bilateral microphthalmia, left retinal detachment, and bilateral optic nerve hypoplasia. At 2 years and 4 months, her height and weight were 81.2 cm (-1.90 SD) and 11.2 kg (+0.73 SD), respectively, and mental development was favorable. Since visual tracking was normal, the left eye was blind and the right eye was thought to be slightly visible. Urinalysis was normal, serum creatinine was 0.42 mg/dL (Cr-eGFR 63.5 mL/min/1.73 m^2), and ultrasonography revealed bilateral hypoplastic kidneys with the right and left kidney lengths of 43.7 mm and 43.5 mm, respectively. She had a normal female karyotype with 46, XX, and whole exome sequencing revealed *de novo* frameshift mutations in *PAX2* and *OPA1*. Additional electroretinogram indicated optic nerve atrophy.
Conclusion: To our knowledge, there have been no reports on cases with mutation in both *PAX2* and *OPA1*. Progressive total blindness in RCS has not been reported, but has been commented on in review articles. The cause of late blindness is unknown in RCS. It may be due to genetic mutations associated with blindness, such as in our case, and electroretinogram should be included in the evaluation of the ophthalmologic examination.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-072 - An unusual genetic diagnosis in a child presenting with end-stage renal disease

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Case report: An 11-year-old girl presented vomiting, fatigue and pale appearance. In her personal history we withhold development coordination disorder, short stature and antenatal diagnosed congenital cystic adenomatoid malformation in the left chest for which lobectomy at the age of 1. Clinical examination demonstrated peripheral edema and malignant hypertension. Initial blood work revealed severe kidney failure (creatinine 11.93 mg/dL; urea 302 mg/dL) presumably present for a longer time as high PTH and low reticulocyte counts in presence of anemia were found. In addition, signs of thrombotic microangiopathy (TMA) with low normal C3, negative screening for verotoxin and normal ADAMST13 were present. Renal ultrasound showed two normal sized kidneys (50th percentile) with hyperechogenic cortex bilaterally and no hydronephrosis. Kidney biopsy revealed significant signs of chronicity (IFTA 9) with TMA, but without arguments for immune complex etiology. After correction of blood pressure, TMA resolved and additional work-up (including genetics) for atypical HUS came back negative.
As no recovery in kidney function was seen while on hemodialysis, she was transitioned to chronic peritoneal dialysis. Additionally, genetic work-up to screen for a broad panel of renal conditions was performed and revealed an unreported *de novo* heterozygous mutation in Cullin 3 (CUL3) (exon 9; c.1349del,p.(Ser450LeufsTer5)), diagnostic for pseudohypoaldosteronism type IIe. While previously published patients with a CUL3 mutation have normal kidney function, this case presented with an atypical severely impacted kidney function. Interestingly, adult mice with an induced tubule-specific CUL3 deletion presented with sustained proximal tubule injury, followed by interstitial inflammation, progressive fibrotic renal disease and death. Therefore, this involvement of CUL3 in kidney injury and fibrosis might – next to malignant hypertension related TMA – also explain the severity of renal impairment in our patient and needs to be addressed in future research.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-073 - A case report of Fabry disease in an asymptomatic 6-year-old boy: the role of kidney biopsy in early diagnosis of renal involvement

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Introduction: Fabry disease (FD) is a rare X-linked disorder caused by absent or deficient lysosomal alpha-galactosidase A (α-Gal A). Pain is a noticeable symptom in children with classical FD; however, renal involvement can be present in asymptomatic children. Thus, a kidney biopsy should be performed in selected cases even before the onset of albuminuria.
Objectives: To report the case of an asymptomatic 6-year-old boy with a family history of Fabry disease.
Description: A six-year-old boy followed at the outpatient clinic due to a family history of Fabry disease had a previous history of pain in limbs upon waking, which improved during the day. This pain did not persist, and he remained asymptomatic. He denied numbness, tingling in the limbs, abdominal pain, or anhidrosis. Physical examination was normal. The albumin/creatinine ratio was 3.1 mg/g and persisted at 5.1mg/g. Creatinine 0.4mg/dL. Electrocardiogram, sinus rhythm, heart rate 84 bpm, QRS axis + 60°, PR interval 0.1 seconds, and no signs of overload. Echocardiogram normal biventricular function. MRI of the skull, renal ultrasound, audiometry, ophthalmologic examination with no alterations. Dosage of lyso-Gb3 6.5ng/mL (< 1.8ng/mL), α-Gal enzyme activity 0.16 µmol/L/h (1.68-13.65 µmol/L/h). Molecular examination showed the presence of a pathogenic variant in homozygous - NM_000169.3(GLA):c.1066C>T;p.(Arg356Trp) in the GLA gene associated with alpha-galactosity A deficiency. In order to program treatment with enzyme replacement, a kidney biopsy was performed. It showed focal lamellar inclusions in podocyte cytoplasm, endothelium, and tubular epithelium, and preserved podocyte pedicels.
Discussion and conclusion: Here, we presented a case of an asymptomatic boy with kidney involvement of Fabry disease, in this case, confirmed through renal biopsy. Early diagnosis in Fabry disease is essential to guide the beginning of treatment with enzyme replacement, aiming to reduce long-term consequences and increase the quality of life.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-074 - A 5q35 deletion including NSD1 and SLC34A1 associated with severe kidney phenotype, proximal tubulopathy, and Sotos syndrome

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Sotos syndrome is characterized by overgrowth, developmental deficits, and characteristic craniofacial features, which is caused by heterozygous variants of the *NSD1* gene located at the chromosome 5q35, and its inheritance mode is autosomal dominant. Kidney phenotypes in this disease include vesicoureteral reflux, hydronephrosis and agenesis. The *SLC34A1* gene also located at the chromosome 5q35, presents infantile hypercalcemia or Fanconi syndrome, and its inheritance mode is typically autosomal recessive. However, monoallelic variants also lead to kidney stone diseases in adulthood. Although the *NSD1* and *SLC34A1* exist contiguously, there are only two cases reported so far who have heterozygous deletions including these two genes.
A 5-month-old boy with Sotos syndrome diagnosed by karyotype analysis for chromosome 5, had also hypercalcemia, hypercalciuria, elevated level of activated vitamin D3, bilateral nephrocalcinosis, low molecular weight proteinuria, kidney enlargement, and chronic kidney disease (Cr-eGFR level was 50-60ml/min/1.73m²). We conducted custom array comparative

genomic hybridization and detected heterozygous microdeletion of 5q35, which include *NSD1* and *SLC34A1*. Although the kidney phenotype was too severe for monoallelic deletion of *SLC34A1* gene, we failed to detect another variant in this gene by genetic sequencing. We also conducted sequencing for other genes causative for proximal tubulopathies such as *OCRL*, *CLCN5* or *HNF4B*, but it was also negative.
The clinical characteristics of the two reported cases are as follows; Case 1 was 6-month-old girl with Sotos syndrome. During follow up, she had bilateral nephrocalcinosis and enlarged kidneys and her serum Cr level increased (Cr 0.49 mg/dL at 3.6-year-old). Case 2 was 10-day-old girl with Sotos syndrome. She had bilateral nephrocalcinosis, and hypercalcemia. During follow up, her serum Cr level increased (Cr 0.52 mg/dL at 1.4-year-old). These facts may suggest contiguous heterozygous deletion of *NSD1* and *SLC34A1* can cause severe kidney phenotypes when compared to heterozygous intragenic *SLC34A1* gene variants.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-075 - Antenatal kidneys hypoplasia reveals a new variant of Townes-Brocks syndrome-1.

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Introduction: Townes-Brocks syndrome-1 (TBS-1) is a rare autosomal dominant disease resulting from *SALL1* gene mutations on chromosome 16q12.1. Phenotypes are variable but commonly combine anorectal (imperforate anus, anal stenosis), external ear (dysplastic ear, preauricular pit or tag) and thumb (triphalangeal thumb or preaxial polydactyly) malformations. Sensorineural hearing loss may also occur. Kidney and urinary tract abnormalities have been reported but never as the main clinical presentation in pediatric TBS-1 syndrome.
Material and methods: We report the case of a TBS-1 newborn affected by kidney impairment and bilateral severe hypoplasia, due to a truncating neomutation in *SALL1* gene.
Results: During pregnancy, a healthy mother was addressed to a pediatric nephrologist for bilateral mildly hyperechoic kidneys hypoplasia (size <P5th). Fetal growth and amniotic fluid were within normal range and no other abnormalities were observed. Birth and initial physical examination were unremarkable except for a right thumb polydactyly. Birth-weight and -length were within the normal range. Postnatal echography confirmed the bilateral renal hypoplasia without other urinary tract abnormalities. Plasma creatinine was 0.46 mg/dL (eGFR by Schwartz formula: 57 ml/min/1.73m2). Audiometric and visual examinations were normal. Early genetic test revealed a *de novo* heterozygous variant in *SALL1* (NM_002968.3): c.838_842del (p.Asn280Leufs*30).
Discussion: *SALL1* encodes an important developmental zinc-finger transcription factor essential to kidney organogenesis. When truncated *SALL1* proteins lack the first double zinc finger (i.e. nucleotides 1351-1497), TBS-1 classical phenotype is usually observed, with hearing loss and malformations of anus and limbs. Our case shows clinical characteristics more compatible to ciliopathies. Kidney structural abnormalities (hypoplasia, dysplasia, polycystic kidneys), sometimes leading to kidney failure, have already been reported but seldom as the main impairment especially during childhood. TBS-1 should be suspected in antenatally diagnosed kidneys hypoplasia.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-076 - The endocannabinoid system mediates cystogenesis in tuberous sclerosis kidney disease

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Introduction: Tuberous Sclerosis Complex disease (TSC) is caused by an inactivating mutation in *TSC* genes. CKD secondary to angiomyolipoma and renal cysts is a leading cause of morbidity in TSC. The endocannabinoid (eCB) system is involved in kidney pathophysiology. Its ligands act mainly through CB1R and CB2R. We aim to explore eCB involvement in TSC cystic kidney disease and its potential role as a therapeutic intervention.
Methods: We used a TSC mouse model Tsc1 deletion in nephron progenitor cells as well as HK2 cell line with TSC1 deletion using Crispr/cas9. eCB system characterization was performed by measuring the expression of its enzymes and receptors using western blotting, immunohistochemistry, and immunofluorescence techniques, along with real-time PCR for RNA expression and liquid chromatography/inline tandem mass spectrometry analysis for ligand level measurements. Manipulation of the eCB system was performed by injecting a CB1R antagonist to pregnant mice bearing Tsc1 null embryos and evaluating their kidneys after birth
Results: eCB ligands level in TSC kidneys changed significantly with an elevation of *N*-arachidonoyl ethanolamide and a decline in 2-arachidonoyl levels compared to control as well as the expression level of enzymes involved in their biosynthesis and degradation. Both expression and protein level of CB1R was higher in the TSC1 mouse model and TSC1 null HK2 cell. Daily IP injection of CB1R antagonist to pregnant females has decreased the cystic burden of TSC1 null offspring compared to control. Furthermore, incubating HK2 cells with CB1R antagonists has prevented LPS-induced increase in TNFα expression, implying an anti-inflammatory mechanism responsible for the beneficial effect of Cb1R antagonists.
Conclusion: TSC1 deletion in the kidney modifies the eCB system, including ligands, enzymes, and receptors profile. Blockage of CB1R in the embryo during pregnancy can prevent TSC cystogenesis. Inflammation may have a role in the beneficial effect of CB1R antagonist in TSC cystic kidney disease.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-077 - X- linked hypophosphatemia (XLH) : the interest of feedback focus groups to assess patients and caregivers' needs

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Background: XLH is a multi-systemic disease requiring a multidisciplinary approach. A specific antiFGF23 antibody was recently approved, thus modifying the management. This led us to envision the creation of a dedicated therapeutic education program for XLH patients.
Methods: A literature search found no specific action in XLH, neither for the patients' specific needs nor for the methodology of patients' evaluation of needs. Thus, to identify the specific needs of XLH patients (children and adults) and their caregivers, and to understand the burden of XLH in daily life, we organized focus groups during a "XLH day" in our reference center for rare diseases of calcium and phosphate metabolism.
Results: Three focus groups were organized, one for XLH children (N=5), one for XLH adults (N=10) and one for caregivers (parents or spouses, N=6). Each group was led by a person trained in therapeutic education (e.g., nurse, pediatric nephrologist, rheumatologist or nephrologist) with another health care provider specialized in XLH. One additional person (e.g., clinical research associate or pediatric resident) with a specific XLH knowledge took minutes. The duration of each session was 1.5 hours, and XLH patients/caregivers were asked to answer age-adapted "open questions" on their daily life and quality of life. Used tools were paperboards and post-its. At the end of the three groups that ran in parallel, a global restitution was made to the entire population at the end of the XLH day. Major needs were identified: dental care, adapted physical activity and nutrition in all age groups, with additional questions on pain management, socio-professional adaptations and financial support in adults. Partner patients were also identified to co-build the support program.
Conclusion: Assessing needs in XLH patients and caregivers using focus groups is a crucial preliminary step to target relevant issues to build a dedicated support program.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-079 - Whole genome sequencing involved sequential diagnosis strategy improved molecular diagnosis of pediatric kidney disease

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Objectives: Genetic disorders contribute significantly to pediatric kidney disease, although combination of targeted or whole exome sequencing (WES) and chromosomal microarray analysis (CMA) in clinical settings, a considerable proportion of patients with suspected hereditary kidney disease are still unsolved. We developed a suitable sequencing strategy to reduce cost and improve diagnostic rate for patients with highly phenotypic heterogeneity. We performed the utility of WGS involved sequential diagnosis strategy in pediatric patients with kidney disease.
Methods: We recruited 141 patients with kidney disease of an underlying genetic disorder from a national pediatric nephrology center, WES (100×) and CMA (3×) are first conducted, we then performed WGS (30×) in individuals without pathogenic variants identified. We finally evaluated WGS data from unsolved cases for likely pathogenic variants using ACMG criteria, and discussed by a group of pediatric nephrology specialists and geneticists.
Results: A total of 141 individuals were enrolled in our study. The median age of the patients at diagnosis was 4.5 years, 61% (87/141) of individuals are male. The specific disease group were 41.8% (59/141) individuals with CAKUT, 37.4% (49/141) individuals with glomerular diseases, 14.9% (21/141) cases with tubular diseases or nephronophthisis, and the remaining 8.5% (12/141) individuals with other kidney disease. By WES and CMA, the molecular diagnostic rate by dWES and CMA is 39.0% (55/141), In the remainder, we performed WGS, and we identified pathogenic variants in 3.6% (5/141) families, which include 4 families with deleterious variants in mitochondrial genes and 1 family with pathogenic CNV specifically.
Conclusions: We firstly evaluated the utility of WGS involved sequential diagnosis strategy in suspected hereditary kidney disease. We show that our sequential diagnosis strategy can increase the molecular diagnostic ratio from 39% (55/141) to 42.6% (60/141). Importantly, our study indicated pathogenic variants in mitochondrial genes plays a major role in pediatric kidney disease.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-081 - A child with diffuse mesangial sclerosis caused by a missense mutation of TRPC6 gene

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Objective: To explore the genetic etiology and follow-up in a child with steroid-resistant nephrotic syndrome and diffuse mesangial sclerosis.
Methods: Genomic DNA was isolated from peripheral blood leukocytes of the proband and his parents. Targeted next generation sequencing and Sanger sequencing were performed in the index, and segregation analyses was performed in the proband's parents.
Results: A heterozygous missense variant in TRPC6 gene [c.325G>A (*p*. Gly109Ser)] was detected in the proband by genetic testing, whereas this variant cannot be traced to his parents. According to the guidelines for the interpretation of sequence variants developed by American College of Medical Genetics and Genomics, this variant was classified as pathogenic.
Conclusion: This is the first report on a missense mutation in TRPC6 gene in a Chinese boy with diffuse mesangial sclerosis, which extends the phenotypic spectrum of this gene.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-082 - Nutcracker syndrome complicated by left vein thrombosis in a patient with protein S deficiency

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Nutcracker syndrome, which defined as compression of the left renal vein between the aorta and the superior mesenteric artery, is usually benign and self-limiting. Long-term renal venous retention can increase the risk of renal vein thrombosis, however, renal vein thrombosis associated with nutcracker syndrome is a rare entity. We present a patient whose complaint of flank pain led to the diagnosis of a renal vein thrombosis and nutcracker syndrome. He was subsequently found to have protein S deficiency. DNA sequence analysis identified a novel, heterozygous, frame-shit mutation in PROS 1 gene (c.166del[p.(Arg56Glufs*31)]. The patient was treated with anticoagulants (first with heparin and then with warfarin) and partial resolution of the renal vein thrombosis with good forward flow from the left renal vein at 2 years of follow up.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-084 - Assessing of the impact of unclassified variants in causative genes that cause Alport syndrome

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Objective: A large number of unknown significance or unclassified variants in *COL4A3*, *COL4A4* and *COL4A5* genes leading to Alport syndrome pose a challenge for genetic diagnosis and subsequent genetic counseling. The aims of this study were to analyze the pathogenicity of unclassified variants in the three causative genes and to make genetic diagnosis of Alport syndrome.
Methods: Six patients clinically diagnosed or suspected of Alport syndrome with unknown significance variants in intron areas or exons in the three causative genes detected by whole exome sequencing were enrolled in the study. mRNA was extracted from patient-derived urine pellets directly and analyzed by reverse-transcription polymerase reaction (RT-PCR) and direct sequencing. Three different prediction tools including HSF, MaxEntScan, and NNSPLIC were used for splice site prediction.
Results: Four patients with Alport syndrome and two patients suspected of Alport syndrome were enrolled in this study. Totally six novel unknown significance variants in the three genes, one for each patient, were analyzed. Of these variants, two were intronic variants in *COL4A3,* three were intronic variants in *COL4A5* and one was a variant of exon in *COL4A5*. Transcript analyses using patient-derived urine pellets revealed all of them affect RNA splicing. *COL4A3*(NM_000091.5)variants c.3211-30G>T and c.828+5G>A resulted in partial intron 37 retention and whole exon 14 skipping respectively, and *COL4A5*(NM_000495.5)variants c.1033-10_1033-2del9, c.4298-20T>A, c.1033-10G>A and c.451A>G caused partial exon 19 skipping, partial intron 46 retention, partial intron 18 retention, and exon 8 skipping, respectively. The six patients in this study were genetic diagnosed with Alport syndrome.
Conclusion: Six novel unclassified variants in causative genes of Alport syndrome were determined as pathogenic variants by analyzing patient-derived urine mRNA, which provides evidence for molecular diagnosis and subsequent genetic counseling in the clinical settings.

Genetics and Genetic Disease (not otherwise more specifically categorised)

P1-085 - The new compound heterozygous mutation of NUP Nephropathy: report of two cases and literature review

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Backgrouds: To explore the relationship between NUP mutation and renal disorders, we provide two cases and a literature review of the genotypical and phenotypical features in patients with NUP nephropathy.
Results: We reported two patients with newly diagnosed NUP nephropathy who carried a compound heterozygous mutations in NUP107 and NUP93 gene respectively. Both patients were diagnosed steroid-resistant nephrotic syndrome and progressed to end-stage renal disease in childhood. While the mutation c.1537+1G>A in NUP93 gene was previously described, the mutations c.460A>G and c.1085C>T in NUP107 gene and c.1472A>T in NUP93 gene were novel. We also summarized the phenotypic and genetic spectrum of NUP nephropathy in eighty-six reported patients who carried 50 different mutations in 6 NUP genes (NUP107, NUP93, NUP205, NUP85, NUP133, NUP160). The majority of them were Asians (66/86, 76.7%). Nephrotic syndrome was the most common renal manifestation (68/86, 79.1%). Although the renal prognosis was poor that 80.8% (59/73) of them developed end-stage renal disease within the first two decades, the outcome of renal transplantation in NUP nephropathy is better than patients with other steroid-resistant nephrotic syndrome. Various extra-renal manifestations were found in 44.8% (26/58) of patients. Neurological involvement was the most common extra-renal presentation (22/26, 84.6%), including microcephaly (13/22, 59.1%), intellectual disability (12/22, 54.5%), and global developmental delay (10/22, 45.5%). Diverse abnormalities of the facial appearance (8/26, 48 30.8%), short stature (5/26, 19.2%), and contain convergent strabismus (4/26, 15.4%) had also been reported. There are significant differences in extra-renal manifestations between different genomics.
Conclusions: The renal manifestation of NUP nephropathy is highly consistent that mostpatients suffered early-onset SRNS with FSGS. More than half of the patients had extra-renal symptom concomitantly. Asians showed potential susceptibility to NUP nephropathy. Despite the limited reports, some genotype-phenotype correlations have been gradually revealed.

Hemolytic uremic syndromes and thrombotic microangiopathy

P1-086 - Validation of peak serum creatinine as the best predictor of long-term renal outcome in non-dialyzed hemolytic uremic syndrome patients.

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Objective: To identify predictors of long-term renal outcome in hemolytic uremic syndrome (HUS) patients non-dialyzed during the acute stage.
Methods: Patients under 18 years old with typical HUS followed for at least 5 years were included. The long-term outcome was evaluated at last control as complete recovery (CR: normal creatinine clearance, neither hypertension nor proteinuria/albuminuria) and different stages of chronic kidney disease (CKD).
Gender, age, leukocytes, hematocrit, hemoglobin and serum creatinine (sCr) at onset, and peak value of sCr, Ardissino's score (hemoglobin + 2 sCr at diagnosis), a new score (hemoglobin + 2 peak sCr) and follow-up time were evaluated as predictors of CKD. The median (Q 1-3) of all variables was compared between patients with CR and those with CKD.
Results: 122 patients, 62 female (51%) with a median age of 19.5 months at HUS diagnosis and a median follow-up of 11 years 4 months (range 5-24 years) were included.

At the last control, 82 (67%) had a CR, 36 (30%) were in CKD stage 1 (13 had significant albuminuria, 21 proteinuria and 2 hypertension), and 4 (3%) had CKD stage 2. No patients were in CKD stage 3-5.
Median values of the initial sCr, peak sCr and the new score showed statistically significant differences between patients with CR and those with CKD 1-2.

Table: Comparison of variables in the acute phase and long-term renal outcome in non-dialyzed patients with hemolytic uremic syndrome.

Renal outcome / Variables	Complete Recovery Median (Q 1-3)	Chronic Kidney Disease stage 1-2 Median (Q 1-3)	P value	N
Age (months)	18.50 (11.75;30.25)	23.50 (11;46)	0.318	122
Leukocytes (cel/mm^3)	13650 (10025;18050)	14450 (11550;18825)	0.547	102
Hematocrit Hto (%)	23 (19.75;29.25)	23 (19.00;25.25)	0.328	80
Hemoglobin Hb (g/dl)	7.75 (6.775;9.825)	7.75 (6.775;8.35)	0.504	80
Serum creatinine sCr (mg/dl)	1.02 (0.70;1.455)	1.77 (0.78;3.29)	0.005	93
Ardissino's score (Hb + 2 sCr)	10.48 (8.32;12.12)	11.64 (9.23;14.49)	0.071	73
New score (Hb + 2 peak sCr)	10.99 (9.41;12.56)	13.20 (9.74;17.95)	0.037	73
Peak sCr (mg/dl)	1.2 (0.87;2.0)	2.42 (1.065;4.65)	0.002	95
Time of follow-up (months)	147.5 (99;187)	135 (91.75;186.75)	0.627	122
Number of patients (%)	82 (67.2%)	40 (32.8%)	-	122

Q1: 1st quartile; Q3: 3rd quartile.

Median peak sCr (mg/dl) was 1.2 (Q 0.87-2) vs. 2.42 (Q 1.065-4.65) in patients with CR and CKD respectively (p= 0.002) with an AUC 0.695 (CI 0.557-0.813).
The best peak sCr cut-off value to distinguish patients at risk of progression to CKD was 1.75 mg/dl (OR 4.632, CI 1.879-11.421; p=0.001).
Conclusion: In HUS patients, not requiring dialysis during the acute stage, peak sCr was the best CKD predictor. Serum Cr over 1.75 mg/dl increased 4.6 times the risk of progression to CKD.

Hemolytic uremic syndromes and thrombotic microangiopathy

P1-087 - An atypical presentation of typical hemolytic uremic syndrome in association with cobalamine deficiency and severe failure to thrive.

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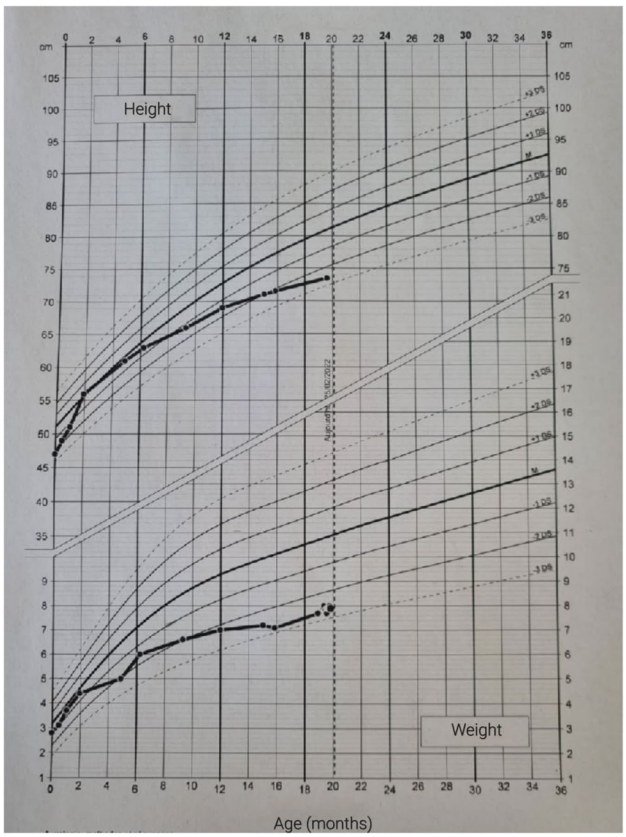
Hemolytic-uremic syndrome (HUS) is one of the main causes of acute kidney injury in children under 5 years of age. It is usually due to Shigatoxin producing Escherichia coli (STEC). While atypical HUS (aHUS) is primarily due to complement dysregulations, other rare etiologies include coenzyme cobalamin (VitB12) metabolic disorders, autoimmune diseases or infections.

A 20 month-old girl, born at term, was admitted for jaundice and brown urine, general distress, constipation and lost appetite. No bloody diarrhea or vomiting was reported.
She presented hypertension and petechiaes. Neurological examination showed hypotonia, poor feeding and global developmental delay. Growth charts revealed a severe failure to thrive (figure1). Further inquiries revealed extended breastfeeding due to difficult weaning.
Exams showed hemolytic anemia, thrombocytopenia, normal complementemia and acute kidney injury associated with proteinuria and hematuria. Suspecting HUS, a stool culture was performed detecting STEC infection. Neuro-MRI was normal. Neurological status and atypical presentation were suspicious for underlying triggers. A metabolic screen was then performed revealing unmeasurable vitamin-B12 and decreased methionine levels. Methylmalonic aciduria and homocystinuria were excluded by aminoacid chromatography. Biermer's disease was ruled-out. Despite anti-transglutaminase antibodies positivity, suggestive for celiac disease, intestinal biopsies were negative. These findings confirmed that cobalamine deficiency was only due to dietary inadequacy, invalidating the hypothesized connection between the neurological status and the HUS.
Our purpose is to raise awareness of the importance of holistic evaluation of patients with HUS, avoiding over-simplification during the diagnostic algorithm. Even in presence of STEC-positivity, nephrologists should recognize red flags such as metabolic anomalies and atypical presentations, which could represent the tip of the iceberg of underlying conditions requiring specific management. As seen in this case report, nowadays, it is very important to provide an appropriate nutritional counseling, especially during the weaning, as pediatric malnutrition can lead to severe consequences.



Hemolytic uremic syndromes and thrombotic microangiopathy
P1-088 - G6PD deficiency: a partner in crime in complement mediated diseases or an "innocent" bystander?

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Introduction: The thrombotic microangiopathies (TMAs) are clinical syndromes defined by thrombocytopenia, nonimmune microangiopathic hemolytic anemia (MAHA), and organ damage. The diagnosis implies a specific pathologic lesion characterized by abnormalities in the endothelium of capillaries and small arteries in association with microvascular thromboses. [CMN1] Defining the underlying pathogenic mechanism of TMAs remains challenging and is critical to determining the optimal therapeutic approach. Here we illustrate a group of patients clinically diagnosed with TMA who carry pathogenic variants in the *G6PD* gene.
Materials and Methods: 511 patients with a clinical diagnosis of TMA were tested for genetic abnormalities using our, locally designed, NGS platform.
Results: Of 511 patients screened, 37 patients were positive for deleterious *G6PD* variants (9 hemizygotes, 3 homozygotes and 25 heterozygotes). All identified variants were either class II (<10% residual G6PD activity) or III (10-60% residual G6PD activity). The variants were identified predominantly in the African American population (26/37). The most common variant identified was the well described "A-" variant. Twelve patients also carried at least one complement gene variant and one patient was co-positive for factor H autoantibodies.
Conclusions: Our findings indicate that approximately 7% of TMA diagnoses may be confounded by genetically programmed G6PD deficiency, the most common enzyme deficiency worldwide. Deficiency of this enzyme is associated with a broad spectrum of diseases, however, is most well-known for causing acute and/or chronic hemolysis. While a clear mechanism has yet to be elucidated (particularly as to how an enzyme deficiency such as this may trigger thrombocytopenia), our data would suggest that G6PD deficiency may also play a role in a clinical presentation that mimics TMA. As many hemolytic episodes relating to G6PD deficiency may be prevented (ie by avoiding triggers), genetic screening for *G6PD* should be included in the clinical setting of TMA.

Hemolytic uremic syndromes and thrombotic microangiopathy
P1-089 - Transient elevation of plasma C5b-9 is not related to transplant-associated thrombotic microangiopathy (TA-TMA) in children treated with allogeneic hematopoietic stem cell transplantation (alloHSCT)

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Introduction: TA-TMA is a severe complication of HSCT, diagnosed in 16% of pediatric patients and predominantly affecting kidneys with mortality reaching 90%. Pathogenetic cornerstone of TA-TMA is complement activation reflected in elevation of C5b-9 blood concentration acting as key factor of endothelial destruction. The aim of the study was to evaluate C5b-C9 concentration in children after alloHSCT with respect to kidney damage and other TMA symptoms.
Material and methods: 35 children aged 0.5-18yr (24 boys and 11girls; 18 with malignant and 17 with non-malignant disorders), transplanted in 2021, were analyzed. Plasma C5b-9 was measured by the EIA method (MicroVue SC5b-9 Plus Enzyme Immunoassay®, Quidel; upper normal range limit 244ng/ml). Samples were taken before conditioning (day -7), and on days 0, and +7, +14, +21, +28, +56, +100 post-alloHSCT. After centrifugation plasma was collected and frozen at -80°C. Symptoms of TA-TMA (anemia, thrombocytopenia, schistocytes in blood smear, elevated LDH, proteinuria, hypertension) were evaluated at the same time. In 14 patients analysis for all timepoints was completed, and in 21 patients sample results from peritransplant period were available.
Results: One patient presented TMA symptoms before conditioning. His C5b-9 plasma concentration on days -7 and 0 were very high (2180 and 1431ng/ml) and decreased to 271ng/ml after eculizumab administration. He died on day +15 due to TMA and sepsis. Ten patients had elevated C5b-9 (8 - once and 2 in two consecutive measurements), but only one of them had transient proteinuria. No differences were found between children with normal and elevated level of C5b-9 in terms of conditioning type, cyclosporin concentration and viral infections.
Conclusions: in this preliminary study the incidence of TA-TMA was low in pediatric alloHSCT population and high plasma C5b-9 correlated with clinical course. Incidental elevation of C5b-9 was common after alloHSCT but normalized spontaneously and didn't precede overt TA-TMA.
Funding: This work was supported by the Saving Kids With Cancer Foundation (grant number FNRD.C200.21.001).

Hemolytic uremic syndromes and thrombotic microangiopathy
P1-090 - A Multicenter Retrospective Study Evaluating the Discontinuation Of Eculizumab Therapy In Children With Atypical Hemolytic Uremic Syndrome

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Background: Atypical hemolytic uremic syndrome (aHUS) is a rare, life-threatening thrombotic microangiopathy (TMA). aHUS has been

treated successfully with eculizumab. The optimal duration of eculizumab treatment in patients with aHUS remains poorly defined.
Methods: We conducted a retrospective multicenter study in the Arabian Gulf Region for children less than 18 years of age, diagnosed with atypical Hemolytic Uremic Syndrome, who discontinue eculizumab therapy, to assess the rate of TMA recurrence as well as the outcome of the patients.
Results: We analyzed 28 patients with clinically diagnosis aHUS who stopped eculizumab. The median duration of eculizumab before discontinuation was 12 months. The most common reason for discontinuation of Eculizumab was complete remission (71.4%), followed by negative genetic testing (28.6%). During a median follow-up period of 24 months after discontinuation, 8/28 patients (28.5%) experienced TMA relapse. Most of the patients (75%) restarted eculizumab within 24- 48 hr. The median time to a TMA relapse after discontinuation was three months. None of the patients with new TMA events required dialysis at the time of relapse. Patients with an increased risk of TMA recurrence had a history of decreased urine output (p=0.002) during initial presentation and positive genetic mutation (p=0.020). The time to relapse of patients with MCP/CD46 mutation was significantly shorter than the other gene mutations. As a long-term outcome after discontinuation, 23 (82.1%) patients were in remission, while 4 (14.3%) patients had chronic kidney disease (CKD), and one (03.6%) case was transplanted.
Conclusions: Discontinuation of eculizumab in patients with aHUS is not without risk; it can result in TMA recurrence. It can be performed with close monitoring of the patients. It is essential to assess risk factors before eculizumab discontinuation. Resuming eculizumab immediately after relapse is crucial and effective in most patients.

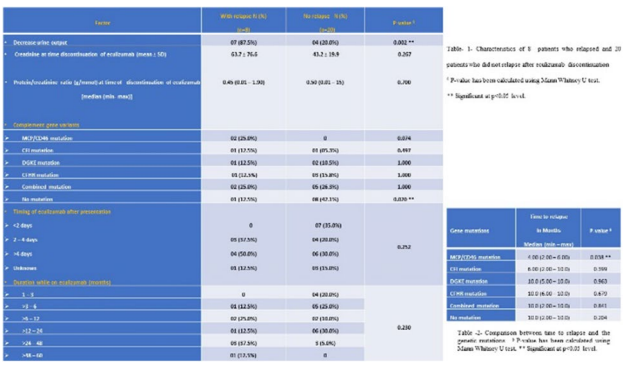

Table- 1- Characteristics of 8 patients who relapsed and 20 patients who did not relapse after eculizumab discontinuation

† P-value has been calculated using Mann Whitney U test.

** Significant at p<0.05 level.

Table -2- Comparison between time to relapse and the genetic mutations † P-value has been calculated using Mann Whitney U test. ** Significant at p<0.05 level.

Hemolytic uremic syndromes and thrombotic microangiopathy
P1-091 - Relapsing atypical hemolytic uremic syndrome

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Background: Atypical hemolytic uremic syndrome (aHUS) is a form of thrombotic microangiopathy (TMA) characterized by a triad of thrombocytopenia, mechanical haemolytic anemia, and acute kidney injury. aHUS has been treated successfully with eculizumab. It is at high risk of relapse at any time. It is well established that infections may precipitate aHUS relapse. Data on the outcome of relapse are limited.
Methods: We performed a retrospective multicenter study in the Arabian Gulf region for children under 18 years of age with relapsing aHUS, to assess the risk factors and the relapse outcome.
Results: Twelve patients were included in this study. Ten (83.3 %) patients developed relapse after eculizumab discontinuation, two (16.6 %) patients relapsed while undergoing maintenance Eculizumab treatment. For those discontinued eculizumab, the most common triggering factors for relapse were upper respiratory tract infection (URTI). COVID-19 infection was the triggering factor in one patient. The possible risk factors for patients who developed relapse during maintenance Eculizumab therapy were severe hypertension, significant proteinuria, and sepsis. Two (16.6 %) patients with relapse required acute dialysis at the time of relapse. As a long-term outcome, 8 (66.6.%) patients were in remission, two (16.6%) patients became chronic kidney disease, one (8.3.%) case was transplanted, one patient died due to relapse and septic shock.
Conclusions: Patients with aHUS are at risk of relapse, particularly after discontinuation of eculizumab or during severe illnesses. To detect early relapse in aHUS, close monitoring of the patients is essential. In this particular disease, resuming eculizumab, higher eculizumab doses and/or shorter intervals to ensure an efficient and sustained blockade seem required.

Table-1- Patient characteristics and outcomes following relapse

*Upper respiratory tract infection , **Acute gastroenteritis.

Hemolytic uremic syndromes and thrombotic microangiopathy

P1-092 - Atypical Hemolytic Uremic Syndrome : Safe switch from eculizumab to ravulizumab

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Introduction: Atypical hemolytic uremic syndrome (aHUS) is a rare entity of thrombotic microangiopathy, characterized by microangiopathic hemolytic anemia, thrombocytopenia, and renal damage,

secondary to overactivation of the alternative pathway of complement. Terminal complement inhibitors, including eculizumab and the ravulizumab, are the approved drugs for aHUS treatment. Ravulizumab was engineered from eculizumab to have an increased half-life allowing for reduced dosing frequency.
Methods: We report two patients with aHUS, who switched from eculizumab to ravulizumab therapy without complications.
Results: Two girls aged 8 and 6 years old respectively were diagnosed with aHUS 3 years ago. Both patients were initially treated with peritoneal dialysis and administration of fresh frozen plasma. Eculizumab therapy was initiated with good clinical response in both patients. Two years later, both patients switched to ravulizumub, permitting extension of dose interval, from 15 days to 4 and 8 weeks respectively. No recurrence of the disease or serious side effects were observed during a 6 month-period in both patients.
Conclusion: Both complement inhibitors eculizumab and ravulizumab appear to be effective and safe in treating aHUS. Based on our experience, switching from eculizumab to ravulizumab seems to be well-tolerated in pediatric patients with aHUS, permitting reduction of dosing frequency, and therefore improvement of life quality.

Hemolytic uremic syndromes and thrombotic microangiopathy

P1-093 - A case of atypical hemolytic syndrome associated with diacylglycerol kinase epsilon mutation (DGKE-aHUS): Re-thinking the treatment with an anti C5 monoclonal therapy.

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Introduction: Atypical Hemolytic Uremic Syndrome (aHUS) is generally caused by dysregulation of the complement cascade; however other causes can lead to aHUS with no complement association. The Diacylglycerol Kinase Epsilon (DGKE) gene, involved in the coagulation pathway, has been recently implicated in several phenotypes of kidney damage, including susceptibility to aHUS and nephrotic syndrome in the first year of life. A loss-of-function mutation in DGKE results in sustained arachidonic acid-containing diacylglycerols (AA-DAG) signaling and PKC activation, creating a prothrombotic state. Here, we present a case of aHUS-DGKE with normal serum C3 levels and transitory treatment with an anti-C5 monoclonal antibody.
Case report: A 9-year-old girl with history of nephrotic syndrome in the first year of life and transitory PD was referred to our Institution. Two kidney biopsies were performed with focal segmental glomerulosclerosis (FSGS) and IFM C3+++, treated with steroids and cyclosporine. At age four she developed TMA receiving Eculizumab for a two-year period, with progression of loss of kidney function. On examination no edema, BP 130/90mmHg (95th percentile), creatinine 1.9mg/dL, albumine 3g/dL, C3 102mg/dL, C4 15.6mg/dL, nephrotic range proteinuria 2gr/d and hematuria. Control kidney biopsy (March 2022) with worsening intersticial fibrosis (grade 3), arteriolar changes and negative IFM.
Discussion: DGKE-aHUS manifested in the first year of life with persistent proteinuria, hematuria, hypertension, and loss of kidney function leading to CKD without an specific treatment. The management for aHUS includes an anti-C5 monoclonal therapy to regulate the complement system. Theoretically, DGKE-aHUS is not complement mediated, however, a small group of patients were previously described with low serum C3 levels and/or C3 deposition in kidney biopsies suggesting a potential role of the complement system. Therefore, we must re-think the treatment with an anti-C5 therapy in these particular phenotypes of DGKE-aHUS.

Hemolytic uremic syndromes and thrombotic microangiopathy

P1-094 - Homozygous mutation of CD46 causing atypical hemolytic uremic syndrome which treatment strategy is the best choice?

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Background: Homozygous mutations in CD46 as the cause of atypical Hemolytic uremic syndrome (aHUS) are very uncommon. Heterozygous individuals often remain asymptomatic or experience a milder course of disease, while homozygous individuals with severely depleted CD46 surface expression might experience more severe disease manifestation.
Methods: Here we describe a family of four with CD46 mutations, diagnosed after the first episode of aHUS in the oldest son.
Results: The index patient had the first episode of aHUS at the age of five, triggered by a viral infection. The episode was mild with no need of hemodialysis. Sequencing revealed a homozygous mutation in the *CD46* gene (c.565T>G, p.Tyr189Asp) previously associated with aHUS . The patient was immunized with relevant vaccinations including meningococcal vaccination in case of future need for Eculizumab. The second episode of aHUS occurred at eight years of age triggered by COVID-19 infection. The patient responded immediately to eculizumab with no need of hemodialysis and his renal function was restored. The younger sibling carrying the same homozygous CD46 mutation is still asymptomatic at the age of three. Both parents are heterozygous for the CD46 mutation and are so far asymptomatic.
There is sparse evidence on how long to treat these patients with Eculizumab. Our protocol based on expert opinion from the ERKNet is the following: Start Eculizumab within 1-2 days of relapse and treat for three months followed by careful monitoring. Treatment on demand is now the plan for future episodes of aHUS for all the family members carrying the CD46 mutation.
Conclusions: aHUS caused by homozygous mutations in CD46 are very seldom and the prognosis not well described. On demand treatment with Eculizimab may be a strategy to preserve kidney function avoiding the possible serious complications of continuous treatment with Eculizumab and save the effective but rather expensive drug.

Hemolytic uremic syndromes and thrombotic microangiopathy

P1-095 - Secondary thrombotic microangiopathy (TMA) in multicentric Castleman disease

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Introduction: Secondary TMAs disorders in pediatric patients are uncommon but have been reported with autoimmune diseases (SLE) and medications (calcineurin inhibitors). Secondary TMA with Castleman disease (CD) is less well recognized. Case studies of adult patients with multicentric CD (mCD) or TAFRO have reported kidney involvement with TMA; along with a single pediatric case report. mCD as a cause for secondary TMAs in children is not well known; the purpose of this case report is to increase awareness of this condition amongst pediatric nephrologists as a differential diagnosis for aHUS.

Results: 6 pediatric patients were diagnosed CD at our institution over a 10 year period (2011-2022). 3/6 (50%) patients had mCD; all patients were noted to have significant proteinuria, edema and evidence of TMA on kidney biopsies. No patient with unicentric CD had renal involvement. All 3 patients presented with fevers, lymphadenopathy, hepatosplenomegaly and edema. Lab findings showed hemolytic anemia with schistocytes, thrombocytopenia along with a significant proteinuria & hypoalbuminemia consistent with nephrotic syndrome. Additional work up is shown below:

Case	ANA	Anti-Cardiolipin	Complement activation	ADAMTS-13	HHV8	Elevated IL-6	Kidney biopsy
#1	Neg	IgM pos IgG neg	Elevated sMAC	>10%	Neg	ü	Active TMA, mesangiolysis
#2	Neg	Neg	n/a	>10%	n/a	ü	Active TMA, mesangiolysis
#3	Pos	Neg	Elevated sMAC	>10%	Neg	ü	Chronic TMA, immune complex GN

2 patients had evidence of AKI and required RRT. On follow up, after targeted therapy, both patients have complete renal recovery and were able to wean off dialysis.

Conclusion: Patients presenting with systemic findings and TMA should be evaluated for CD given the association and response to targeted therapy. The mechanism of TMA in CD remains unclear but may be due to direct endothelial injury or complement activation, as ADAMTS-13 deficiency was not noted in our patient population.

Hemolytic uremic syndromes and thrombotic microangiopathy

P1-096 - Severe Central Nervous System (CNS) involvement in STEC-HUS

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Introduction: Severe CNS disease is related to acute morbidity and mortality in STEC-HUS.

Objectives: 1) to characterize the clinicopathologic features; 2) to evaluate the severity of renal and colonic disease; 3) to evaluate mortality rate; 4) to evaluate long term kidney outcome.

Material and Methods: retrospective study (Sept 2011-Oct 2021) of STEC-HUS and severe CNS disease.

Inclusion criteria: ≥ 3 seizures, stupor, coma, ventilator mechanical assistance (VMA) requirement. We evaluated: age, prodromal diarrhea, status of hydration, arterial hypertension (HT), hemorrhagic colitis (HC), RRT, CNS disease (VMA, anticonvulsants, CT scan and EEG), laboratory findings, mortality. At last follow up, creatinine clearance, albuminuria, HT.

Results: 193 STEC-HUS assisted, 26 (13.5%) with severe CNS disease. Mean age 42.8 mo. All presented diarrhea, 5/26 dehydrated, 5/26 overhydrated and 4/26 hypertensive. 12/26 presented ≥ 3 seizures, 24/26 needed VMA, mean 8.8 days, 21/26 recibed anticonvulsants. 8/13 EEG abnormal. CNS CT scans (9/26) normal in 5, ischemic findings 4. HC in 19/26 (12 surgery, 2 intestinal resections). 25/26 required RRT, mean 14 days. Mean laboratory evaluations: WBC 30,500/mm3 (r: 5,200-74,700), hematocrit 30.8% (r: 16-42), platelets 81,900/mm3 (r: 20,000-250,000), albumin 25.4 g/l (r: 12.2-33.3), Na 130.6 mEq/l (r: 119-144), creatinine 3.67 mg/dl (r: 1.3-7.3), urea 1.68 g/l (r: 0.69-3.5). 11 exhibited hyperglycemia, 2 diabetes. Three patients died during first week, one in second week (4/26 deaths, 15.3 %). Mean follow up 59 mo (r: 1-117). Six patients los follow up. At last visit, 9 normal kidney function, 4 albuminuria +/- HT, 2 CKD stage 3, 1 ESKD.

Conclusions: Severe CNS disease presented in 13.5%, half with ≥ 3 seizures and 90% required VMA. It was associated with HC and RRT requirements. Mortality rate is 3- 5 times higher than that reported for the whole STEC-HUS population. Almost half of the patients showed renal disease on follow up.

Hemolytic uremic syndromes and thrombotic microangiopathy

P1-097 - Efficacy of abbreviated plasma exchanges (PEX) in anti-factor H (anti-FH) associated atypical hemolytic uremic syndrome (aHUS)

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Objective: PEX and immunosuppression are the mainstay of management of anti-FH aHUS. While the duration of therapy with PEX for anti-FH aHUS is empirical, longer sessions are associated with adverse events.

Methods: We compared the efficacy of abbreviated PEX protocol (10-12 sessions over 3-weeks) in a prospective cohort of patients <18-yr-old (2020-22; n=20), to the standard PEX protocol (20-22 sessions over 5-weeks) in a historic cohort (2016-19; n=65). Efficacy was defined as fall in anti-FH titers by 70% or ≤1300 AU/ml on day 28 of initiating PEX. Patients also received prednisolone and 5-6 pulses of cyclophosphamide followed by mycophenolate mofetil. We compared hematological remission, fall in anti-FH titers and adverse kidney outcomes (stage-2 hypertension, urine protein/creatinine >1mg/mg, eGFR <60 ml/min/1.73m^2) at 3 and 6-months follow-up.

Results: Of 20 patients, aged 7.6±2.5 years**,** PEX could be abbreviated in 16 (80%) patients to 11.5±3.3 sessions. Abbreviation failed due to no hematological remission after day-14 of starting PEX (n=3) and catheter-related infection (n=1). Anti-FH levels at presentation

and day-14 in 4 patients in whom PEX was not abbreviated were similar (P>0.1). **Table** shows parameters at onset and sequentially in the patients undergoing abbreviated PEX. The percentage fall in anti-FH with abbreviated versus standard PEX at 1, 3 and 6-months from onset were similar (85±14% vs. 89±12%; 74±33% vs. 86±19% and 76±25% vs. 86±14%, respectively, P>0.1). The proportion of patients with adverse kidney outcomes in patients undergoing abbreviated vs. standard PEX at 6-months was 50% vs. 67% (P=0.21).
Conclusion: Abbreviation of duration of PEX to 10-12 sessions is feasible and efficacious in reducing anti-FH titers; careful monitoring for ongoing hemolysis is required. Short-term outcomes are comparable to the historical cohort undergoing PEX for 20-22 sessions.

Table. Markers of disease activity [median (IQR) or mean ± SD] in patients on abbreviated PEX.

Parameter	Onset (n=20)	1 month (n=16)	3 months (n=16)	6 months (n=16)
Hemoglobin, g/dL	6.4±1.5	9.2±1.9	11.2±1.8	11.2±1.7
Platelets, *10^3/µL	84.5 (49,133)	226 (207,259)	266 (180,325)	227 (196,294)
eGFR, ml/min/1.73m^2	13.8 (0.2,19.0)	46.6 (20.9,77.8)	80.1 (50.4,112.3)	70.7 (50.9,93.6)
LDH, U/L	1230 (1060,1831)	311 (255,423)	350 (285,547)	299 (251,350)
Up/Uc, mg/mg	2.7 (2.1,6.2)	4.5 (0.8,5.9)	1.2 (0.5,1.8)	0.6 (0.4,1.5)
C3, mg/mL	76.8±6.9	109±20.8	112±20.1	114±12.8
Anti-FH, AU/ml	2683 (1598,6288)	406 (225,605)	375 (169,846)	630 (169,782)
Reduction of antiFH from baseline, %		88.4±12.9	74.1±33.1	76.8±25.7

Hemolytic uremic syndromes and thrombotic microangiopathy

P1-098 - Eculizumab in shiga toxin-producing escherichia coli haemolytic uraemic syndrome (STEC-HUS) with severe neurological involvement

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Introduction: The role of Eculizumab in atypical haemolytic uraemic syndrome is well established across the literature. To date, there is little published pertaining to the role of this therapy in STEC-HUS. Central nervous system (CNS) involvement can be associated with STEC-HUS. There remains controversy on the optimal management of these sick children. We present a case series of n=4 patients, with CNS involvement of STEC-HUS, treated with Eculizumab.
Methods: Retrospective chart review was conducted of four patients with severe neurological sequelae of STEC-HUS, managed with Eculizumab infusion at our centre. All patients were evaluated by a consultant paediatric neurologist, prior to and following the commencement of therapy.
Results: Four patients (75% female) were admitted to our national paediatric nephrology centre with severe CNS involvement of STEC-HUS in 2021. The median age was 59 months (IQR 23.5-105.5) and the median weight was 18.5kg (IQR 11.65-28.9). The constellation of neurological symptoms experienced by each patient varied, they included: Ataxia; blurry vision; hypotonia; hyperreflexia; nystagmus; eye twitching/rolling; strabismus; seizures; confusion; lip smacking; decreased level of consciousness. Three patients (75%) required PICU admission. One patient required haemodialysis (25%) and one required peritoneal dialysis (25%). All patients received 2 doses of Eculizumab, one week apart (dosing according to weight). All patients underwent MRI and have documented abnormal neuroimaging during their illness. Three of four (75%) patients have shown complete renal/neurological recovery at six-month follow-up.
Conclusion: We present a clinical case series of four children with STEC-HUS and associated severe neurological involvement, managed with Eculizumab only, in lieu of plasma exchange (as per our previous policy). The marked improvement in symptoms in these cases merits further consideration for the therapeutic benefit for complement blockade in STEC-HUS.

Hypertension

P1-101 - A case of acute heart failure with a rare renal cause

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Background: Not treated High blood pressure (HBP) in children could lead to acute heart failure (AHF). The rarest causes of HBP must be taken into consideration when a patient presents a such clinical condition.

Clinical case presentation: We present a case of a 12 years old child hospitalised for shortness of breath, palpitations (NYHA II dyspnea), thoracic pain and tachycardia with normal EKG. For 4 months he had malaise and flashes with high blood pressure episodes. The ejection fraction was low (30%) and had a mitral valve regurgitation. He was diagnosed with AHF and treatment was started. When he was stable he developed rapidly arterial hypertension (170/120mmHg). Investigations showed elevated plasma and urine catecholamines. A PET-scan was run and a 7 cm left lombo-aortic paraganglioma was found.
Clinical evolution and echography imaging were improving after initiation of the treatment, but delaying the diagnosis also postponed the surgery of the pheochromocytoma by four months because his cardiac insufficiency could not permit it. He underwent laparoscopic surgery and the tumor was removed. Unfortunately, in the ICU, when decreasing Noradrenaline (from 2000 µg/l at 1000 µg/l) he underwent two episodes of cardiac arrest with ventricular fibrillation (long QT). He had a favourable outcome, he is now treated by Nadolol and Enalapril, with normal blood pressure, and normal cardiac echography. Genetic tests are ongoing.
Conclusion: Paragangliomas (pheochromocytomas) are very rare tumors in children, 40% of them have a genetic transmission. These tumors synthetize, metabolise and secrete catecholamines that can cause symptomatic cardio-vascular clinical manifestations. In case of heart cardiac failure in adolescents we must not forget the causes of high blood pressure.

Hypertension

P1-102 - A confounding case of hypertension in an infant: when you hear hoofbeats think of horses, not zebras

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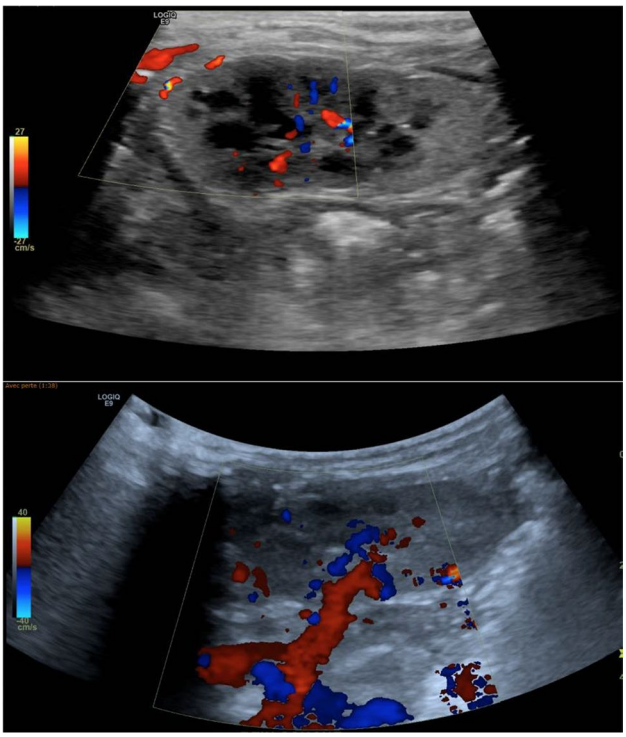
Hypertension in children can be life-threatening and is often undiagnosed or untreated leading to an increased risk of cardiac diseases. In this setting, the main etiologies are renovascular and renal parenchymal or cardiovascular diseases. Diagnosis and treatment are still challenging and the etiology often remains unknown.
A six week-old boy with previous pre-eclampsia and intrauterine growth restriction was admitted for poor feeding and gastroesophageal reflux. The mother had a history of acquired thrombotic thrombocytopenic purpura (aTTP). He presented poor general conditions and polypnea associated with malignant hypertension. Cardiac ultrasound showed dilated cardiomyopathy without aortic coarctation. Abdominal ultrasound was normal with no pyloric stenosis or genitourinary tract abnormalities. Laboratory tests were suggestive for thrombotic microangiopathy and acute kidney injury with hypokalemia. Differential diagnosis focused on a neonatal form of aTTP hypothetically driven by maternal transmission of autoantibodies. Plasma infusion was promptly performed while evaluation of underlying conditions was pending.
Despite the normalization of platelets count, hypertension remained poorly controlled and a cardiogenic shock requiring invasive supports occurred. ADAMTS13 activity and antibodies then returned normal/negative and no circulating antibodies were retrospectively detected in the mother during pregnancy nor post-partum.
Concomitantly the patient presented multiple catheter-related thrombosis with a normal thrombophilia screening. An accurate renal Doppler ultrasound showed a bilateral narrowing of arteries with parenchymal hypoperfusion and a vascularization pattern suspicious for old left renal artery thrombosis(*figure 1*).Thrombophilic status is still unclear, specific evaluations, including genetic testing, are ongoing. Blood pressure is now well-controlled with optimized antihypertensive therapy and anticoagulation. The biological sign of hemolysis have resolved.
This case illustrates that hypertension can have an atypical presentation and be a severe life-threatening condition in young children.
We aim to remind that physicians should primarily rule-out common etiologies before seeking for zebras.



Hypertension

P1-103 - Variation in paediatric 24-hr ambulatory blood pressure monitoring interpretation by Canadian and UK physicians

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Background: 24-hr ambulatory blood pressure monitoring (ABPM) is widely accepted as a more accurate method for measurement of blood pressure (BP) compared to a single office-based measurement of BP. However, it is unclear how physicians interpret ABPM and make management decisions. This study's goal is to investigate variation in ABPM interpretation among paediatric nephrologists (Canada and UK) and paediatric cardiologists (Canada only) via an online survey.
Methods: The survey content included baseline demographics, questions on the use and indications for ABPM, interpretation of results, and subsequent management decisions in various clinical scenarios.
Results: The survey was sent to 196 Canadian physicians, with 69 (35.2%) total responses. Thirty-five UK clinicians also completed the survey. Most respondents were >44 years old, were in practice for at least 11 years, and were university-based. There were substantial differences among clinicians in ABPM interpretation for isolated systolic,

diastolic, and night-time hypertension. For example, only 53.1% of physicians would initiate or modify treatment in those with diastolic HTN in CKD. Further, even for the same abnormal ABPM parameter, the decision to start or alter treatment was influenced by the underlying medical condition (Figure below)
Conclusions: There is significant variation in clinical practice among physicians for interpretation and management of hypertension when using ABPM. Differences in guidelines among various jurisdictions, as well as knowledge gaps in the research on which guidelines are based, creates ambiguity regarding ABPM interpretation and management decisions. A more protocolized approach and further insight into the reasoning behind the variation in physicians' interpretation may help to standardize practice.
Figure: *Canadian paediatric nephrologists' alteration to treatment by ABPM parameter and underlying diagnosis. (N=26)*

Hypertension

P1-104 - Causes of Hypertension at a Children's Hospital in Cape Town, South Africa

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Background: Traditionally hypertension in children is due to secondary causes. With the onset of the obesity epidemic, primary hypertension has become increasingly more common.
Methods: A retrospective medical record review of children < 18years old diagnosed with persistent hypertension in the paediatric nephrology unit at Red Cross Children's Hospital from January 2000 - December 2019.
Results: 156 children were enrolled in the study (115 children in the second decade). The mean age at presentation was 7years 6 months. Overall, 112 children (72%) had secondary hypertension. Only 3 patients (7.5%) had primary hypertension in the first decade. In the second decade 41 of 115 (35%) children had primary hypertension of which 19 (46%) were obese. The commonest presentation at diagnosis, was stage 2 hypertension in all age groups. Fifty five percent of patients were 6-12 years of age. Glomerulopathy (24%), renovascular disease (23%) and obstructive uropathy (9%) were the commonest causes of secondary hypertension. In the children with secondary hypertension, the majority (54%) were also in the 6-12year old age group. Hereditary cystic disease (36%) was the commonest cause of hypertension in children <1 year of age.
Conclusion: There was an increase in the number of children referred to our clinic over the decades. Much of the increase is due to an increase of referral of patients with primary hypertension. A large percentage of these children are obese. Secondary hypertension still remains more common. The causes of hypertension in our setting were similar when compared internationally, except in infants.

Hypertension

P1-105 - Time to Consider 24-hour ABPM's as Standard of Care in Youth Living with Type 2 Diabetes: A cross-sectional study

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Background: Youth living with type 2 diabetes (T2D) are at high risk for hypertension (HTN), however screening with gold-standard 24-hour ambulatory blood pressure (BP) monitoring (ABPM) is rare. We aimed to determine rates of HTN and associations with renal outcomes in youth with T2D.
Methods: A cross-sectional study of youth with T2D in the improving renal Complications in Adolescents with type 2 diabetes through REsearch (iCARE) cohort study with ABPM data. BP was defined as daytime HTN (+/- nocturnal) (daytime mean >95th%ile + BP load >25%); isolated nocturnal HTN (normal daytime BP, sleep mean >95th%ile + BP load >25% OR dipping <10%) or normal. Outcomes included non-orthostatic urine albumin:creatinine ratio (ACR) and eGFR. Multivariate regression analyses tested for associations between BP type and outcomes.
Results: A total of 277 youth had ABPM data; age 14.69 ± 2.06 yrs, duration of T2D 2.17 ± 1.78 yrs, 84.1% First Nation ancestry. In total n=55(19.6%) had daytime ± nocturnal HTN, n=80(28.5%) had isolated nocturnal HTN and n=142(51.2%) had normal BP. ACR was positively associated with daytime HTN (ß=0.553;p=0.001), duration of T2D (ß=0.857;p=0.02), HbA1c (ß=1.172;p=<0.0001) and ACEI/ARB use (ß=3.94;p<0.0001); (R^2=0.184). Age, sex, BMI-z score, nocturnal HTN, other antihypertensive use was not associated with ACR. In contrast, HTN status was not associated with eGFR (ß=-1.856;p=0.28), but with age (ß=2.11;p=<0.0001), sex (ß=17.81;p=<0.0001), BMI-z-score (ß=12.88;p<0.0001) and HbA1c (ß=1.72;p=<0.0001); model R^2 = 0.553.
Conclusions: Daytime and isolated nocturnal HTN are common in youth with T2D early in their disease course. In this cross-sectional analysis daytime hypertension was associated with ACR, the earliest clinical marker of diabetic kidney disease (DKD). More study is required to determine optimal clinical targets to delay progression over time. Due to the high prevalence of HTN, routine use of ABPMs should be considered in routine clinical care.2

Hypertension

P1-106 - Yield of diagnostic testing in evaluating etiology of pediatric hypertension

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Objective: Current guideline recommendations regarding the utility of diagnostic investigations for pediatric hypertension are based on limited evidence, leading to wide variation in practice for the diagnostic workup. The objective of this study is to characterize the cohort of children that may benefit from secondary hypertension workup, and to determine the diagnostic utility of various investigations.

Methods: This was a single center, retrospective review of 169 children aged 1-18 years with elevated blood pressure or hypertension seen at a tertiary pediatric nephrology clinic in Canada, between 2000-2015. The number of tests completed, abnormal test findings, and contributory test results that helped establish hypertension etiology was determined for commonly ordered diagnostic tests. Subgroup analysis was completed based on age of presentation and overweight/obesity status.
Results: Overall, 61 children were diagnosed with primary hypertension, and 100 children with secondary hypertension. Secondary hypertension is the predominant form of hypertension in all ages except in obese adolescents ≥12 years. Half of children with traditional risk factors for primary hypertension, including obesity, were diagnosed with secondary hypertension. Renal ultrasound had the highest yield of diagnostic results (16.4%), with no difference in yield between age groups (P = 0.19). Lipid profile was contributory towards diagnosis of primary hypertension in 11.7% and was only abnormal in overweight/obese children. All other bloodwork investigations had a low yield of contributory results. Echocardiogram had a high yield for identification of target organ effects in hypertensive children (21.9%).
Conclusion: A simplified secondary hypertension workup should be considered for all hypertensive children and adolescents. First line investigation could include a renal ultrasound for all hypertensive children and a lipid profile for overweight/obese children. Echocardiograms for assessment of end organ damage could be considered at diagnosis. Further testing should be considered based on the clinical scenario and results of initial testing for the most cost-effective management.

Hypertension

P1-107 - Left ventricular remodelling in children with primary hypertension

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Objective: left ventricular (LV) remodeling is an important consequence of primary hypertension (PH). Adult studies suggest, the type of LV geometry has significant prognostic value. We present review of studies analyzing LV geometry and determinants of different types of LV remodeling in children and young people (up to 21 years of age) with PH.
Methods: All eligible studies in PubMed database up to January 1st 2022 were included to analysis if they reported both LV geometry and multivariable regression for remodelling pattern.
Results: Eight out of 42 reviewed studies including 2309 children (age range 6-23 years, 60% male) were selected. The prevalence of LV concentric hypertrophy (CH) was in a range of 9.3 - 32%, that of concentric remodelling (CR) 4.6-42 % and eccentric hypertrophy (EH) 5-37%. Three studies reported independent association of systolic (SBP) and diastolic blood pressure (DBP) two of SBP load and BMI with CH. Independent associations with CH were insulin resistance markers (2 studies), oxidative stress (1 study) and visceral obesity (2 studies). One study each reported independent association between BMI and concentric remodeling and one study found that Afro-American race and obesity determined abnormal LV geometry not specifying form of remodelling. EH associated with BMI and less severe stages of PH. Only one study analyzed change of LV geometry during antihypertensive therapy and revealed that prevalence of EH decreased from 37% to 18% while the prevalence of CH did not change significantly. The main determinant relative wall thickness (RWT) reduction was increase of insulin sensitivity.
Conclusions: Elevated BP, obesity and metabolic abnormalities with insulin resistance determine LV geometry in children and adolescents with PH. Normalization of metabolic abnormalities was found to be the main determinant of decrease of RWT but only one study analyzed the effects of treatment. However, analyzed studies used different diagnostic criteria.

Hypertension

P1-108 - Bilateral renal arteries fibromuscular dysplasia: a rare cause of hypertension in children (a case report)

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Introduction: Renal artery fibromuscular dysplasia is a noninflammatory, nonatherosclerotic vasculopathy that can affect renal arteries at various degrees with different severity. The etiology is still unknown. The main presentation is a sudden onset of recalcitrant hypertension at a young age, which is usually resistant to medical treatment. Here we describe a case of bilateral renal artery fibromuscular dysplasia in a Tunisian child
Observation: A 14-year-old boy was referred to our department with an end stage renal disease. he had a history of several hospitalisations for severe hypertension, the initial etiologic screening was negative. His hypertension was difficult to manage, with the need of four antihypertensive medications, hence the decline of his renal function. Renal ultrasound, performed twice, showed a reduced kidney size, without evidence of vascular stenosis. Plasma renin activity was normal, with elevated aldosterone level 572 µmol/l. Proteinuria was 10,8 mg/kg/d. Echocardiography as well as endocrine tests were normal. Renal arteries angio-tomography showed a bilateral renal artery fibromuscular dysplasia. L'évolution était marquée par une difficulté à équilibrer la TA nécessitant une quadrithérapie. The patient was put on haemodialysis allowing a better control of his resistant hypertension.
Conclusion: Renal artery fibromuscular dysplasia is a rare cause of paediatric hypertension, it should be suspected in presence of severe pharmaco-resistant hypertension.

Hypertension

P1-109 - The effect of blood pressure increase on the course of pulse wave velocity in pediatric kidney transplant recipients

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Pulse wave velocity (PWV), indicating arterial stiffness, is a marker of cardiovascular damage and -in adults- predictive of cardiovascular mortality. PWV and blood pressure (BP) changes in children after kidney transplantation (KTx) were investigated to determine to which extent a certain BP increase contributes to higher PWV.

70 children at least 2.5 years after KTx with ≥ 2 PWV measurements were included (follow-up 4±2 years) resulting in 211 observations. Changes of systolic (ΔSBP) and diastolic BP (ΔDBP) were classified into "stable", "1-10mmHg increase" and ">10mmHg increase". Linear mixed modeling for PWV z-score (PWVz) adjusted for ΔSBP and ΔDBP was performed. Additionally, we investigated an extended dataset from 35 patients with monthly entries of BP, immunosuppressive trough levels, and estimated glomerular filtration rates (eGFR), with a total of 2,137 observations, using linear mixed modeling for SBP and DBP z-score.

PWVz increased by 0.11/year (p<0.001). Compared to the "stable" group, PWVz was higher in children with 1-10mmHg BP increase (SBP β=0.57; p=0.046, DBP β=0.85, p<0.001; Table 1). A BP increase of >10mmHg was associated with an even higher PWVz increase (SBP β=0.78, p=0.009; DBP β=1.31, p<0.001). Independent of BP changes, higher PWVz was shown in girls and in children with lower eGFR. An association with underlying disease was seen in the model for ΔSBP (Table 1).

The extended subgroup analysis showed higher DBP z-scores to be associated with younger age, higher BMI, and higher cyclosporine A and everolimus trough levels. No associations with sex, eGFR or tacrolimus trough level were detected.

An alarming surge in arterial stiffness depending on greater BP increases is seen in pediatric KTx recipients. Our data not only points out the central role of adequate BP control in this patient group, but also highlights that controlling modifiable risk factors can improve cardiovascular outcome after KTx.

Table 1a:
Factors associated with PWV z-score, by category of **SBP increase**

Variable	β	SE	p
Age (years)	0.050	0.04	0.259
BMI (kg/m²)	-0.044	0.04	0.278
Female sex (Ref: male sex)	**0.551**	**0.27**	**0.049**
CAKUT (Ref: non-CAKUT)	**-0.547**	**0.26**	**0.044**
eGFR (mL/min/1.73m²)	**-0.009**	**0.01**	**0.046**
SBP at inclusion (mmHg)	0.019	0.01	0.179
Δ – SBP (mmHg)			
Stable / Decreasing (Ref)	-	-	-
Increase 1-10 mmHg	**0.589**	**0.28**	**0.034**
Increase >10 mmHg	**0.779**	**0.28**	**0.007**

Table 1b:
Factors associated with PWV z-score, by category of **DBP increase**

Variable	β	SE	p
Age (years)	0.038	0.04	0.297
BMI (kg/m²)	-0.051	0.03	0.122
Female sex (Ref: male sex)	**0.570**	**0.22**	**0.013**
CAKUT (Ref: non-CAKUT)	-0.406	0.21	0.059
eGFR (mL/min/1.73m²)	-0.008	0.004	0.053
DBP at inclusion (mmHg)	**0.047**	**0.01**	**<.001**
Δ – DBP (mmHg)			
Stable / Decreasing (Ref)	-	-	-
Increase 1-10 mmHg	**0.862**	**0.22**	**<.001**
Increase >10 mmHg	**1.367**	**0.29**	**<.001**

Abbreviations: BMI, body mass index; CAKUT, congenital anomaly of the kidney and urinary tract; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; PWV, pulse wave velocity; SBP, systolic blood pressure; SE, standard error

Hypertension

P1-110 - Isolated ambulatory diastolic hypertension in children - prevalence and impact

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Background: The impact of isolated systolic (iSH) and combined (SDH) ambulatory hypertension has been described; however, less is known about ambulatory isolated diastolic hypertension (iDH), and its association with increased left ventricular mass index (LVMi).
Objectives: To analyze the prevalence of ambulatory iDH in children (1-18 years), and associations with BMI Z-score (BMIz) and LVMi.
Methods: We enrolled 2050 pediatric patients from 4 academic centres who were worked up for primary or secondary hypertension (PH or SH). All patients had ambulatory blood pressure monitoring (ABPM). Ambulatory (daytime, nighttime, 24-hour) iDH was defined as diastolic BP Z-score (DBPz)>1.65, with systolic BP Z-score (SBPz) <=1.65. 1037/2050 had LVMi (g/m^2.7) adjusted to the 95th percentile (aLVMi; Khoury *et al*).
Results: ABPM distributions were: **24-h** iSH 23%, iDH 4.5%, SDH 15%; **daytime** iSH 14%, iDH 2.7%, SDH 8.2%; **nighttime** iSH 13%, iDH 6.8% and SDH 16%. The prevalence of 24-h iDH and daytime iDH was similar in PH (3.6%, 1.9%) and SH (5.2%, 3.5%). However, the prevalence of nighttime iDH was significantly lower in PH (3.9%) vs. SH (9.3%) (p=0.00001). Median aLVMi in children with iDH was not different between PH and SH. However, 30% (95%CI 16-43%) of SH children with nighttime iDH had target organ damage (TOD) (aLVMi > 1), as compared to 14% (95%CI 0-33%) of PH children with nighttime iDH. Children with PH and nighttime iDH had lower aLVMi compared to those with PH and nighttime iSH (p=0.02) or nighttime SDH (p=0.04). Children with PH and nighttime iDH also had lower BMIz as compared to children with PH and nighttime iSH (p=0.04).
Conclusions: In summary, the prevalence of ambulatory iDH is low, but can be as high as ~10% in SH. Children with PH and iDH tend to have lower BMIz and aLVMi, compared to iSH and SDH.

Hypertension

P1-111 - Reliability of blood pressure measured by parents in young children at Home using hand-held Doppler device and aneroid sphygmomanometer for systolic Blood Pressure Measurement (HDBPM)

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Objective: Our objectives in this clinical study were to evaluate the reliability of systolic BP values measured at home by parents of children aged <5 years (Home-$SBP_{Doppler}$) over a 2-week period; and (ii) to compare Home-$SBP_{Doppler}$ with doppler systolic BP measured in clinic by health professional in the hospital at a single visit (Office-$SBP_{Doppler}$).
Design and Methods: At the time of an educational session, we taught parents to measure systolic BP and assessed their technique using a hand-held doppler device and aneroid sphygmomanometer. Using doppler device and BP instrument, we requested parents to perform three consecutive BP measurements twice daily (ideally morning and evening around similar times) when the child was awake, settled and cooperative.

Results: HDBPM measurements were available for 48 children, mean age ± SD of 2.2±1.5 years and 29% on antihypertensive medication. Office-$SBP_{Doppler}$ was 3.0±8.8 mmHg higher than Home-$SBP_{Doppler}$ (P=0.41 between means). Six children displayed a marked white coat effect with Office-$SBP_{Doppler}$ >10 mmHg higher than Home-$SBP_{Doppler}$, of whom five were under 18 months. Excluding these patients from the analysis reduced the mean difference between Office-$SBP_{Doppler}$ and Home-$SBP_{Doppler}$ to 0.6±6.5 mmHg (P=0.82). Mean SBP was similar between week 1 and week 2 HDBPM measurements with 0.15±3.77 mmHg difference between week 1 and week 2 readings (P=0.85). Morning HDBPM measurements were lower than evening with mean difference -2.48±3.84 mmHg, although this difference did not achieve significance (P=0.18). Mean BP differences shown in **Figure 1**.

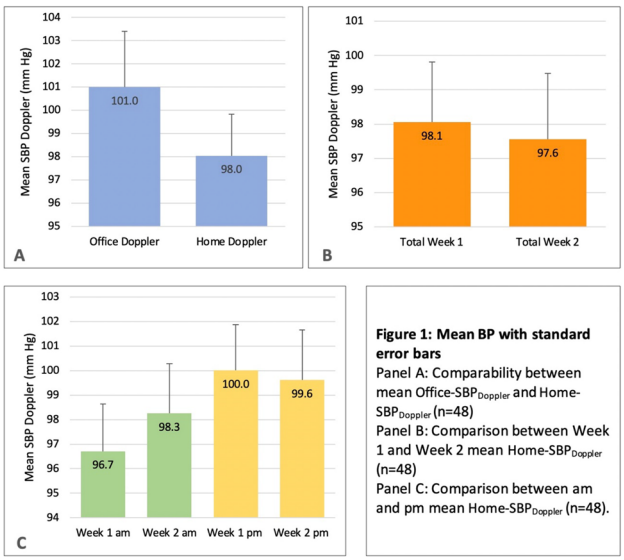

Figure 1: Mean BP with standard error bars
Panel A: Comparability between mean Office-$SBP_{Doppler}$ and Home-$SBP_{Doppler}$ (n=48)
Panel B: Comparison between Week 1 and Week 2 mean Home-$SBP_{Doppler}$ (n=48)
Panel C: Comparison between am and pm mean Home-$SBP_{Doppler}$ (n=48).

Conclusions: Similar to older children, young children show a white coat effect and variation of BP levels through the day. HDBPM is a reliable method for measuring systolic BP in young children with BP levels comparable to those performed by health professional in clinic.

Hypertension

P1-112 - Measurement of systolic BP using a hand-held Doppler device and aneroid sphygmomanometer in children: comparison with office-based auscultatory SBP measurement

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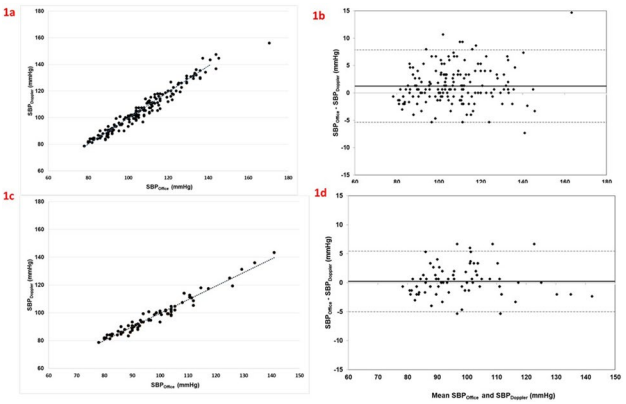
Objective: To compare values of office systolic BP (SBP_{Office}) and systolic BP measured using doppler device ($SBP_{Doppler}$) by health professional in the hospital at a single visit.
Design and Methods: In quick succession, following office BP measurement by auscultation, a hand-held doppler device and the same aneroid sphygmomanometer and cuff were used to measure SBP by the health professional. The mean of three BP values was used.

Results: Single centre observational study including n=180 children, median (interquartile range) 4.95 (2.32, 11.77) years, including n=91 <5years. SBP obtained by health professional in the hospital using doppler device were highly correlated with manual office measurement, SBP_{Office} vs. $SBP_{Doppler}$ (r= 0.975, P<0.001; **Fig 1a & 1c** for all patients and <5 years respectively). The mean SBP_{Office} was 106.4 ± 16.2 mmHg and mean $SBP_{Doppler}$ was 105.1 ± 15.7 mmHg. For those <5 years, mean SBP_{Office} was 97.3 ± 12.6 mmHg and mean $SBP_{Doppler}$ was 97.1 ± 12.5 mmHg. Bland–Altman analysis revealed a small difference in the estimation of SBP by the two methods [**Fig1b & 1d** for all patients and <5 years respectively]. The difference in absolute values between the SBP_{Office} and $SBP_{Doppler}$ was 1.26 ± 3.4mmHg [95% confidence interval (CI), 0.76 to 1.75, P=0.455] and 0.23 ± 2.7mmHg [95% confidence interval (CI), -0.32 to 0.77, P=0.904] for all patients and <5 years respectively. The coefficient of variation for $SBP_{Doppler}$ was less than 2.3%, suggesting excellent repeatability of measurements.
Figure 1:



Conclusions: These data suggest that across the childhood age range, including the youngest children, the mean difference was low with a low SD reflecting good agreement between these methods (auscultation and doppler device) when measured in clinic by health professional. Our results, therefore, suggest that SBP can be determined by hand-held doppler device with similar accuracy to the "reference" auscultatory method.

Hypertension

P1-113 - Isolated systolic hypertension is associated with increased left ventricular mass index and aortic stiffness in adolescents – a CMR study

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Objectives: Despite the high prevalence of isolated systolic hypertension (ISH) among hypertensive adolescents, its clinical significance is not determined. Additionally, it is hypothesized that ISH with normal central blood pressure (BP) in young patients is a benign phenomenon and was hence labelled spurious hypertension (sHTN).

Methods: Using cardiovascular magnetic resonance (CMR) we evaluated a group of 73 patients with suspected primary hypertension, aged 13-17 years (median: 16.9, IQR 15.8-17.4; 13 girls), in whom, based on 24-hour ambulatory BP monitoring (ABPM) either ISH (n=30) or white coat hypertension (WCH) (n=43) was diagnosed. Based on noninvasive central BP measurement 13 participants in the ISH group were classified as having sHTN and 17 were diagnosed with true hypertension (tHTN).
Results: Compared with WCH adolescents, ISH subjects presented with higher indexed left ventricular mass index (LVMI) (p<0.001), maximal left ventricular (LV) wall thickness (p<0.001), LV concentricity (p=0.001) and more often had LV hypertrophy (LVH) (47% vs 14%, p=0.002). They had higher average pulse wave velocity (PWV) in the proximal aorta (p=0.016) and the whole thoracic aorta (p=0.008). Additionally, we observed higher indexed LV stroke volume (p=0.025) in patients with ISH. The sHTN subgroup had significantly higher LVMI and aortic PWV, and more often had LVH compared to the WCH group. The sHTN and tHTN subgroups did not differ in terms of aortic PWV, LVMI or LV geometry.
Conclusions: Compared to adolescents with WCH patients with ISH, including the sHTN subtype, have more pronounced markers of cardiac end-organ damage, higher aortic stiffness and stroke volume.

Hypertension

P1-114 - Comparison of performance of Office, Home and Ambulatory blood pressure monitoring in obese children and their correlation with end organ damage

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Introduction: Ambulatory blood pressure monitoring (ABPM) is regarded as the gold standard for diagnosis and monitoring of hypertension but availability of equipment and skilled healthcare professionals limits the use of ABPM in developing countries like India. Home BP (HBP) is often advised to characterize hypertension, though only few of the studies have compared the diagnostic utility of HBP as compared to office BP and ABPM.
Methods: In this cross-sectional study, 60 obese children underwent ABPM, HBP and office BP (OBP) monitoring along with evaluation for end organ damage. OBP in each visit (minimum of 3 over different occasions) and 7 days HBP monitoring along with ABPM was done. All were screened for end organ damage.
Results: 40 obese children (66.7% male and 33.3% female) with mean age 10.72 ± 2.84 underwent OBP, HBPM and ABPM monitoring. 41.7% had ambulatory HTN; 12(20.0%) were found to be hypertensive on HBP (sensitivity 32%, specificity 86.6%%) and 22(36.7%) were hypertensive on OBP monitoring (sensitivity 64% and 82.8% specificity). WCH and masked hypertension was present in 13.3 % and 18.3%respectively. Study found 28 % of children with severe ambulatory hypertension and 16(26.7%) children with end organ damage. On multivariate analysis showed hypertensive status ABPM and HBPM were independently associated with end organ damage with higher odds ratio for hypertensive status on ABPM (46.03(7.5-910)) compared to HBPM (5.19(1.27-22.76)).
Conclusion: 24 Hour ABPM is the reference standard and is essential for BP monitoring and accurate classification specially in children with high-risk condition. Diagnostic performance of HBPM monitoring is not comparable with ABPM and is less specific in identifying children with white coat and masked hypertension. HBPM is complimentary to rather than an alternative to ABPM to obtain better profile regarding the BP of the child. Ambulatory blood pressure monitoring has strong association with end organ damage.

Hypertension

P1-115 - Clinical manifestations and precipitating factors of hypertensive crisis in pediatric patients

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Background: Hypertensive crisis is an emergency condition in children. Precipitating factors associated with the hypertensive crisis in children have not been widely reported in the current data. The study aimed to focus on clinical presentations and precipitating factors of hypertensive crisis.
Material and method: This retrospective study from 2014 to 2021 in pediatric patients with the hypertensive crisis at Tertiary care hospital of Thailand. We excluded those who had severe hypertension immediately after surgical operation or incomplete medical records. We divided the patients into hypertensive emergency and urgency groups to compare the demographic data, precipitating factors, clinical manifestations, and treatment outcomes.
Results: Of the total 84 episodes of the hypertensive crisis were found eligible for this study. There were 40 hypertensive emergency and 44 hypertensive urgency episodes. The median age was 13.2 years (IQR 10.1, 14.6). Renal disease was the underlying disease of hypertension which lupus nephritis was the major cause. Neurological symptoms were the most common manifestation of hypertensive crisis (53.6%). Seizure, intracranial hemorrhage, and alteration of consciousness were found particularly in a hypertensive emergency. The worsening of underlying disease, volume overload, and poor medication adherence were the three main leading precipitating factors in hypertensive crisis episodes, 36.9%, 29.8%, and 27.4%, respectively. In subgroup analysis between a single episode of hypertensive crisis group versus a recurrent group, found that the poor medication adherence affected mostly in recurrent hypertensive urgency group with statistically significant (71.4%, p=0.005), whereas volume overload had a higher incidence in the recurrent hypertensive emergency group (60%, p=0.009). The mortality rate was 1.2%.
Conclusion: The worsening of underlying disease, poor medication compliance, and volume overload were the most precipitating factors in hypertensive crisis episodes. Neurological symptoms were significant warning signs for early management to prevent a serious complication.

Hypertension

P1-116 - Microalbuminuria in obese and overweight children

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Background: Microalbuminuria is regarded as a predictor of renal damage in obese and overweight children. Hypertension, diabetes, dyslipidemia in obese/overweight children have injurious impact upon kidney.
Objective: To find out frequency, risk factors and association of microalbuminuria in obese and overweight children.
Methods: This cross sectional study was carried out in the Department of Pediatrics and Pediatric Endocrinology in two tertiary care hospitals of Dhaka, Bangladesh from January 2020 to June 2021. Seventy seven obese and overweight children with age ranges 5.5 year to 18 years were included. After proper history and physical evaluation, blood test for sugar, lipid profile, insulin resistance (HOMA-IR), thyroid and renal function were done. Study subjects were divided into two groups based upon the presence of microalbuminuria and different variables of interest were analyzed with appropriate statistical tools.
Result: Study revealed 16.4% of obese and overweight children had undisclosed microalbuminuria. Microalbuminuria was significantly associated with higher BMI and waist circumference (p value <0.001). Seven and half percent of study children had hypertension but diastolic hypertension had significant microalbuminuria (P= 0.028). Low HDL (40.3%) and high triglyceride (38.8%) abnormalities were found in dyslipidemia patients, though it was statistically insignificant. Fasting insulin and HOMA-IR were significantly higher in microalbumunuric obese and overweight subjects. HOMA-IR was found high in 100% subjects with microalbuminuria. Morbid obese and abdominal obesity had significant (P<0.001) microalbuminuria. Multivariate logistic regression analysis showed abdominal obesity as a strong predictor (odds ratio 15.815) of microalbuminuria in obese and overweight children.
Conclusion: Obese and overweight children found to have hypertension, low HDL, high triglyceride, insulin resistance, and had higher incidence of microalbuminuria. Abdominal obesity is an independent risk factor for microalbuminuria in these population.

Hypertension

P1-117 - The impact of blood pressure and body mass index on heart structure and function in adolescents

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Introduction: The purpose was to assess the impact of high blood pressure (BP), blood pressure load (BPL), and body mass index (BMI) on heart structure and function in a cohort of adolescents using echocardiography.
Methods: The data of adolescents examined due to suspected arterial hypertension (AH) were reviewed. Patients diagnosed with secondary AH were excluded. The following clinical and sonographic parameters were collected: BMI, average systolic and diastolic BP (SDB and DBP), and systolic and diastolic BPL (SDBL and DBPL) recorded with 48-hour ambulatory blood pressure monitoring (ABPM). Routinely performed echocardiogram measurements (M mode) included the assessment of the interventricular septal thickness (IVSD), posterior wall thickness (PWTD), and left ventricular internal dimension at end-diastole (LVDD). The left ventricular ejection fraction (EF), left ventricular mass index (LVMI) and left ventricular mass (LVM) were calculated. The ratio of early and late diastolic peak flow (E/A), and peak transmitral ejection velocity to early mitral annular velocity (E/e') were evaluated.
Results: Thirty adolescents aged 13 to 18,5 years were included. Nineteen adolescents had confirmed AH, 10 had prehypertension. Our results showed that BMI, SBP, DBP, SBPL and DBPL have no impact on LVM, EF, and E/e'. IVSD was significantly thicker in adolescents with higher BMI (p=0,039). PWTD showed a tendency to be thicker with higher BMI, although not significantly (p=0,055). The E/A was significantly decreased with higher BMI (p=0,002), and there was a significant increase of LVMI in those patients with higher average SBP (p=0,037). LVDD was significantly increased in adolescents with higher SBP (p=0,039) and nearly significantly increased in those with higher SBPL (p=0,051).
Conclusion: Our findings confirm a considerable impact of elevated blood pressure on the heart, especially on its structure. However, the impact of BMI on heart structure and diastolic function is not negligible. Blood pressure and weight control are therefore essential in adolescents.

Hypertension

P1-118 - Longitudinal ABPM diagnosis in children with chronic kidney disease: CKiD Experience

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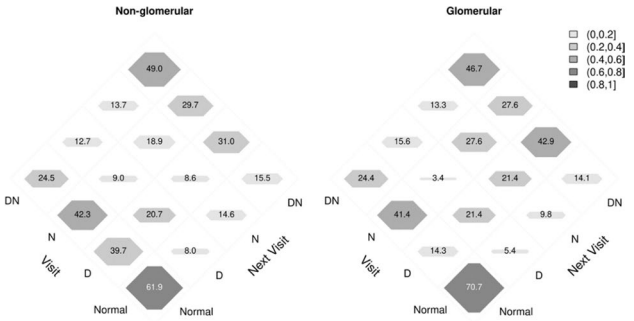
We evaluated persistence of ambulatory blood pressure (ABP) pattern among 464 children (358 with non glomerular [NG] and 106 with glomerular [G]) who underwent a total of 876 pairs of monitorings (ABPM) in the CKiD study. Per protocol, ABPM are separated by 2 years. Hypertension was defined as mean SBP or DBP ≥95% or load >25% during day (D), night (N), or both (DN). D and N determined by wake-sleep diaries. ABPM normal only if both mean & load were <95% during D and N. Approximately half (216) participants contributed only 2 studies, while remainder had either 3 (138), 4 (66), 5 (34), or even 6 (10) ABP studies.

# ABPM studies	G (106)	Non-G (358)	All (464)
	N (%)	N (%)	N (%)
2	58 (54.7)	158 (44.1)	216 (46.6)
3	30 (28.3)	108 (30.2)	138 (29.7)
4	11 (10.4)	55 (15.4)	66 (14.2)
5	6 (5.6)	28 (7.8)	34 (7.3)
6	1 (0.1)	9 (2.5)	10 (2.2)

In 430 (49%) of 876 paired ABPM, the baseline and follow up patterns were the same diagnosis; 265 of 410 (65%) with normal ABPM were still normal while 316 of the 466 (68%) with abnormal ABPM still had abnormal BP at follow up. There was less persistence among those with either D or N hypertension, though they were still likely to have abnormal BP. Half with DN hypertension persisted; 75% remained abnormal at follow up.

		Prior Visit				
		Normal	D	N	DN	Totals
	Normal	265	31	56	63	415
Next visit	D	25	15	8	24	72
	N	59	11	29	41	140
	DN	61	33	34	121	249
Totals		410	90	127	249	876



Among children with CKD who had repeat ABPMs over several years, overall ABP diagnosis (normal versus abnormal) persisted in most cases, suggesting incomplete attention to BP management among hypertensive subjects.

Hypertension

P1-119 - Inadequate dipping on Ambulatory Blood Pressure Monitoring in Children with Solitary Functioning Kidney_ A pilot study

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Solitary functioning kidney (SFK) is an important cause of glomerular hyperfiltration which may result in proteinuria, hypertension (HT) and progression to chronic kidney disease (CKD). Early detection and treatment of HT can delay progression of renal dysfunction. In comparison to office blood pressure (BP) measurement, 24-hour ambulatory blood pressure monitoring (ABPM) is preferred for *diagnosis* of HT in certain conditions. The aim of this study was to determine whether ABPM is superior to office BP in identifying HT in children with SFK. Additionally, to (i) look for hemodynamic and cardiovascular consequences of HT (ii) evaluate for microalbuminuria.

Methods: Children between the ages of 5-18 years, height greater than 120 cms, were enrolled if they were not on antihypertensives, and had a SFK based on history of nephrectomy or a scintigraphy showing a solitary functioning kidney or function less than 10% in 1 of 2 kidneys. Office BP was recorded by an oscillometric method (Omron) and 24-hour ABPM was measured using a Schiller BD 102 apparatus. Standard guidelines (AAP (2017) and AHA (2014)) were followed for measurement and interpretation of office and ABPM respectively. Other investigations performed: urine for sediments and microalbuminuria (UACR: 30-300 mg/g), serum creatinine and ultrasonography of kidneys (compensatory hypertrophy renal length > 95th centile for age). Two-dimensional echocardiography and fundus examination were planned for children diagnosed with HT. Standard deviation scores (SDS) were calculated based on appropriate reference values (anthropometric for Indian children, office BP (AAP 2017) and ABPM parameters (LMS, WUHL 2002), Sub-analyses between congenital and acquired etiologies was performed.

Results: Table 1. Significantly, 2 patients had systolic and diastolic non-dipping and 2 had only diastolic non-dipping. One of the latter also had pre-hypertension on office BP.

Conclusion: Insufficient dipping found in this cohort emphasises the advantage of ABPM over office BP in children with SFK.

Table 1

Baseline characteristics and Blood Pressure profile of all Patients and sub analysis of congenital and acquired SFK

Parameter	All patients N=14	Congenital SFK n=7	Acquired n=7
No. of males (%)	10 (71)	5 (71)	5 (71)
Mean age (years)	9.39	10.14	8.64
Mean height SDS	- 0.4258	- 0.96	- 0.1
Mean weight SDS	- 0.38	-1.017	- 0.2515
Mean BMI SDS	-0.5	0.9	0
Serum creatinine (mg/dl) [mean ± SD]	0.57 (0.10)	0.6 (0.11)	0.54 (0.10)
Mean eGFR (modified Schwartz) (ml/min/1.73m²) [mean ± SD]	97.1 (17.98)	92 (13.72)	102.2 (21.25)
No. with microalbuminuria	0	0	0
No. with compensatory renal hypertrophy (%)	9 (64)	3 (22)	6 (42)
Office BP Values			
Mean Systolic BP SDS	0.05	-0.06	0.17
Mean Diastolic BP SDS	0.44	0.18	0.70
24-hour ABPM values			
24-hour Systolic BP mean SDS	1.08	0.99	1.18
24-hour Diastolic BP mean SDS	0.77	0.87	0.67
Day Systolic BP mean SDS	1.52	1.44	1.60
Day Diastolic BP mean SDS	1.30	1.34	1.27
Night Systolic BP mean SDS	0.01	0.02	0.00
Night Diastolic BP mean SDS	0.61	0.41	0.80
Mean 24-hour Systolic BP Load (%)	9.47	10.78	8.17
Mean 24-hour Diastolic BP Load (%)	10.57	10.44	11.07
No. with Insufficient Dipping (%)	**4 (28.6)**	**2 (14.3)**	**2 (14.3)**

SDS: standard deviation score
Ambulatory BP SD scores were estimated by using reference data of healthy children by the LMS

Hypertension

P1-120 - Risk of Elevated Left Ventricular Mass Index in Children with Masked Hypertension: A Systematic Review and Meta-Analysis

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Background: Masked hypertension (MH) is defined as an elevated ambulatory blood pressure in presence of normal office blood pressure (BP) and is common in children with diabetes, chronic kidney disease (CKD) and obesity. The relationship between adult-onset masked

hypertension (HTN) and subclinical-cardiovascular outcomes (SCOs) have been established; however, the risk of children with MH developing SCOs have not been extensively studied. In the review, we investigate the differences of left ventricular mass index (LVMI) between masked hypertensive and normotensive children.

Methods: A systematic literature search was conducted on four electronic databases to include relevant full-length publications, published abstracts and conference proceedings written in English from Jan 1974 to Mar 2021. Article, data extraction and quality assessment were independently completed and verified by two reviewers. Reported mean LVMI data of MH and normotensive (NTN) subjects was extracted.

Results: Of 8996 screened studies, 12 studies and 2028 total subjects (age range 10-18 years) were included for analysis. MH data for various co-morbid conditions including diabetes, CKD and specific kidney diseases was also collected. LVMI was elevated in the MH group (Adjusted Mean=34.93 $g/m^{-2.7}$) when compared to the NTN group (Adjusted Mean=30.10 $g/m^{-2.7}$). The mean difference in LVMI was 4.05 $g/m^{-2.7}$ (95% CI: 2.77 – 5.33). Meta-regression to investigate the effect size of body mass Index could not be conducted due to limited reporting in studies.

Conclusion: The results from this review demonstrate the impact of MH on elevated LVMI and emphasize the importance of early identification and treatment of MH in children with various comorbid conditions.

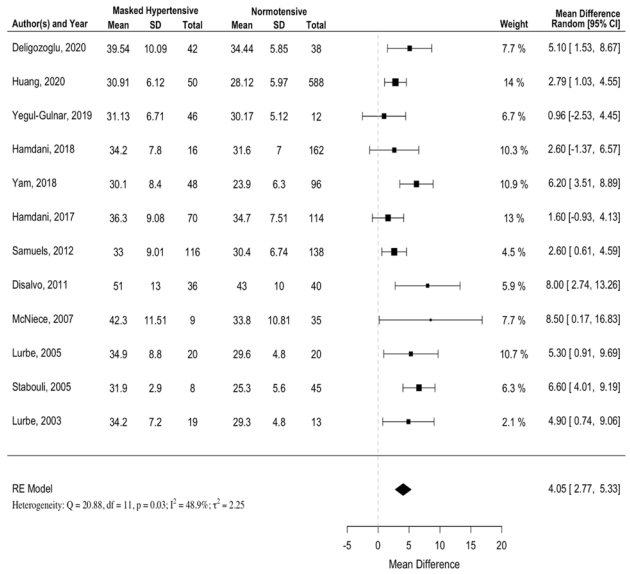

Figure 1: Mean differences in Left Ventricular Mass Index between Masked Hypertensive and Normotensive Children

Hypertension

P1-121 - Prevalence of Masked Hypertension in Children: A Systematic Review and Meta-Analysis

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Background: Masked hypertension (MH) is defined as an elevated ambulatory blood pressure (BP) in presence of normal office BP and is common in children with chronic kidney disease, obesity and congenital heart disease. MH is a known risk factor for target organ damage and adult cardiovascular disease. However, the prevalence of MH in children is unknown. Early identification of patients with abnormal BP is important to delay cardiovascular events. In this review, we determined the prevalence of MH in children with various co-morbid conditions.

Methods: A systematic literature search was conducted on five electronic databases to include relevant full-length publications, published abstracts and conference proceedings written in English from Jan 1990 to Jan 2021. Article screening, data extraction and quality assessment was independently completed by two reviewers and verified by a third reviewer. The prevalence of pediatric MH (<21 Years) was stratified by health status and disease group.

Results: Of 892 studies screened, 124 studies and 24,642 total children (range 8-18 years) were included for final analysis. Healthy participants were defined as children with normal office BP and no co-morbid conditions. MH prevalence was stratified into the following groups: healthy (MH=8.33%), solid organ transplant (MH=25.2%), congenital cardiac conditions (e.g. coarctation of the aorta) (MH=23.47%), chronic dialysis (MH=18.59%), obesity (MH=17.27%), glomerular disease (MH=15.86%) and others. Compared to healthy children, glomerular disease (OR=2.04 p<0.001), organ transplant (OR=2.54, p<0.001), obesity (OR=1.87, p=0.001) and congenital cardiac patients (OR=2.58, p=0.006) had the highest prevalence of MH.

Conclusion: Children with glomerular disease, solid organ transplant, obesity and congenital cardiac disease are at increased risk for MH. Given the prognostic value of MH for predicting adulthood cardiovascular morbidity, its identification and treatment is imperative in at-risk children. Future research should investigate the prevalence of target organ damage in children with MH.

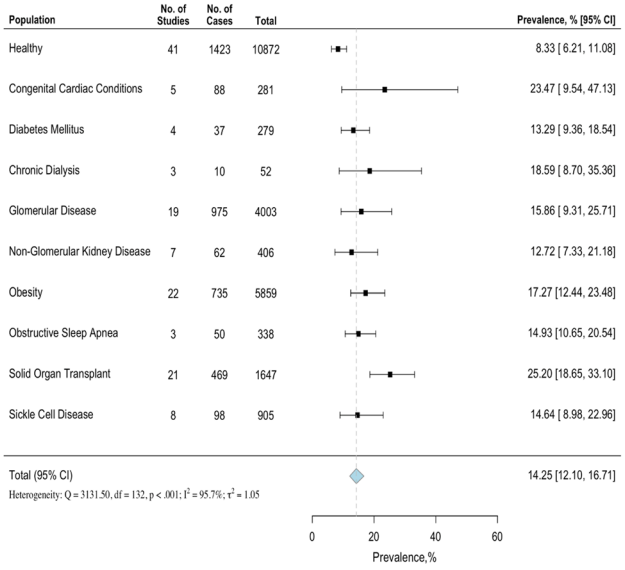

Figure 1. Prevalence of Masked Hypertension in Children, stratified by health condition.

Hypertension

P1-122 - To study prevalence of hypertension and its association with body mass index in children presenting to tertiary care hospital.

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Introduction: Hypertension (HT) is prevalent in about 4-8% of children and is linked to obesity.
Aim: To study prevalence of HT and its association with body mass index (BMI) in children coming to tertiary care centre.
Material
Study Design: Cross sectional observational study.
Subjects: Successive children between age 3y to 18y presenting to hospital in last six months. Known cases with hypertension were excluded.
Methods: Personal history (physical activity/ diet), BMI, BP (oscillometric method; abnormal BP confirmed by auscultatory method) noted, interpreted as per Flynn J et al, 2017. Statistical tests applied for checking correlation between BMI and BP.
Results: Total number of children enrolled n= 377; boys (n=216, 57.3%) girls (n=161, 42.7%)
Children in age 3y-5y (n= 86, 22.8%), 5y-12y (n= 150, 39.8%), 13y-18y (n= 141, 37.4%)
Total prevalence of abnormal BP (elevated BP + HT) (38/377; 10%); elevated BP (n=18, 4.8%); HT (n=20, 5.3%). Of these Stage 1 HT (n=14, 3.7%), Stage 2 HT (n=6, 1.6%).
Boys (7.4%) have higher prevalence of HTN than girls (2.5%).
Children with underweight (n= 17, 4.5%), normal (n= 245, 65%), overweight (n= 62, 16.4%), obese (n= 53, 14.1%). Adiposity (n= 52, 13.8%).
50% cases (n=19) with abnormal BP had high BMI
16.7% cases in age 3y-5y, (1/6, p= 0.358), 27.3% cases in age 5y-12y (13/48, p=0.001), 23.2%, cases in age 13y-18y (13/56 p= 0.007) with high BMI had abnormal BP.
HTN was more common in 5y – 12y (n= 9/13, 69%) compared to 13y -18y (n=3/13, 23%).
5.9% of underweight children had abnormal BP.
Conclusion: 10% of total children had BP abnormal BP.
There seems to be direct correlation between high BMI and high BP.
Lifestyle modifications and weight control should be specifically advised to children in 5y-12 y in order to control HT.

Hypertension

P1-123 - Non-invasive paediatric blood pressure assessment: exploring the clinicians' perspective.

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Obtaining accurate and reliable blood pressure (BP) readings in paediatric patients is challenging, given inadequate guideline adherence, limited device validation, and patient stress.
Aim: This study aimed to investigate clinicians' perspectives surrounding non-invasive paediatric BP assessment to identify opportunities for improvements to BP technology and clinical practice.
Method: In this qualitative study based on an adaptation of the extended Technology Acceptance Model (TAM2), semi-structured interviews (n=20) were conducted with clinicians involved in non-invasive paediatric BP assessment in in-patient and out-patient settings of a tertiary/quaternary paediatric hospital e.g. cardiology outpatient clinic, cardiac and renal inpatient ward, and hospital in the home (HITH). Deductive analyses based on TAM2, and inductive thematic analyses for additional themes, were conducted.
Results: Clinician responses (n=20) demonstrated that a major hindrance to reliable paediatric BP assessment is poor tolerability of BP measurement due to excessive cuff inflation. Clinicians described low trust in BP readings from automated devices, often related to poor tolerability. Limited trust in BP readings led reduced utility for informing treatment decisions. Clinicians expressed greater trust in readings from auscultatory measurement, which was better tolerated, but expressed that performing manual assessment is inconvenient.
Conclusion: A dissonance exists between 1) low trust and clinical utility of the most common BP measurement approach (automated), versus 2) higher trust and clinical utility, but efficiency and user-related impediments, for the auscultatory method. Based on our results, we have developed the Blood Pressure Acceptance Model (BPAM), which can be used to explain and predict clinicians' use of BP technology. Further work is needed to improve tolerability and accuracy of automated BP devices in real-world paediatric settings.

Hypertension

P1-126 - Hyponatremic hypertensive syndrome in a 4year old Nigerian boy with right renal artery stenosis: Treatment delay.

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Background: Hyponatremic hypertensive syndrome (HHS) is characterized by malignant hypertension, hyponatremia, hypokalemia secondary to unilateral renal artery stenosis. HHS a common presentation in adults with renovascular hypertension is rare in children. We report the case of a 4year old male presenting with HHS with delay in the definitive treatment.
Case Report: A 4year old male presented with a history of recurrent headache and vomiting of 8 months, excessive thirst and frequent urination of 5 months. On examination he was conscious and alert, he had elevated blood pressure of 200/140mmHg. Other systemic findings were essentially normal.
Urinalysis showed proteinuria (+), Serum electrolytes showed hyponatremia ranging between 109- 124mmol/l, hypokalemia between 2.6-3.2mmol/l within the 1st 48hours, normal Urea (2.9 - 4.6mmol/l) and elevated Creatinine of 140µmol/l. Repeat creatinine after 72hrs was 55umol/l. Urine osmolality 263.6mOsm/kg, Serum osmolality 263 nmol/l, Serum Cortisol 440nmol/l. Renal ultrasound scan showed Left Kidney measuring 9.43 x 4.59 x 2.65cm, Right Kidney was 7.01cm x 2.69 x 2.65cm with good echotexture and corticomedullary

differentiation. CT Angiography confirmed right renal artery stenosis. Brain MRI and Echocardiography were normal.
He received sublingual nifedipine, IV hydralazine and labetolol initially and was subsequently maintained on tabs hydralazine, atenolol and amlodipine with fair blood pressure control with BP ranging between 140-100- 120/80mmHg while awaiting right renal artery angioplasty which could not be done due to unavailability of cardiac catheterization laboratory in most centers in Nigeria and lack of appropriate paediatric catheter in the only cardiac center with cardiac cath lab. The child is still on follow up in our clinic.
Conclusion: HHS is a rare and serious complication of renovascular hypertension which can occur in children. Lack of facilities for renal artery angioplasty in our environment has delayed the management of this child with risk of morbidity and mortality from severe hypertension and end stage renal disease.

Hypertension

P1-127 - Extensive review of pharmacokinetic and pharmacodynamic properties of ACE-inhibitors and angiotensin receptor blockers in hypertensive children

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Background/Aims: Globally, hypertension is among the key preventable causes of premature death. Currently, childhood hypertension is estimated around 2 to 4% of the paediatric population. The leading cause for childhood hypertension is renal impairment, described in over 90% of the Western cases. ACE-inhibitors (ACE-I) and Angiotensin Receptor Blockers (ARBs) are most frequently prescribed for blood pressure reduction. Both therapeutics are currently being used largely off-label due to a lack of appropriate study design and results, despite being on the market for over three decades.
Method: This review focused on the clinical trials investigating pharmacokinetic and pharmacodynamic properties of ACE-I and ARBs over the past 30 years in response to regulatory initiatives. A total of 60 studies were selected, including 3660 hypertensive children. Analysis was conducted with a focus on trial design and endpoints, drug dosing, safety, efficacy and drug indication.
Results: Between ACE-I and ARBs, geographical location, drug intake and formulations were comparable. Study population differed, where studies on ARBs focused on both primary and secondary hypertension, whereas studies on ACE-I focused on secondary hypertension. Sampling regimens differed, where studies investigating the PK of ARBs were more frequently based on single dosing at non-steady state. For both classes, low reporting of estimated glomerular filtration rate (eGFR) (23.3%) was apparent. Individual antihypertensive effects of ACE-I could be verified in only 77 children, where around 90% achieved a blood pressure decrease of $\geq$ 6 mmHg. ACE-I and ARBs were generally well tolerated when considering safety parameters and serious adverse events.
Conclusion: Standardization of methodology and reporting of results is imperative for both PK and PD studies, to allow a better comparison of results and to aim towards appropriate labelling. Stratification for and inclusion of different age categories and eGFR ranges is recommended.

Hypertension

P1-128 - Population pharmacokinetics and Bayesian estimations of lisinopril at steady state in hypertensive children with mild to moderate renal impairment

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Objective: Lisinopril, an angiotensin-converting enzyme (ACE) inhibitor, is the most frequently prescribed antihypertensive drug in the pediatric population. The drug is used off-label and PK/PD data are only available in children with normal GFR Lisinopril pharmacokinetics was studied in renally impaired, hypertensive pediatric patients, corresponding to the majority of the day-to-day clinical pediatric population.
Methods: The lisinopril pilot study included 13 children with primary to secondary hypertension who received oral lisinopril once daily, doses ranging from 0.05 mg/kg to 0.2 mg/kg. A total of 46 peak and trough plasma samples were collected. Patients were aged between 1.9 and 17.9 years (median 13.5 years) and weight ranged between 9.62 and 97.2 kg (median 53.2 kg). Estimated glomerular filtration rate (eGFR) was measured between 55.5 and 180 mL/min/1.73m2 (median 99.9 ml/min/1.73m2). Model building was performed based on improvement in objective function values, goodness-of-fit evaluations, prediction corrected visual predictive checks, convergence assessments and parsimony. All data were analyzed using Monolix version 2020R1 (Lixoft®, France) and R version 3.6.2.
Results: A one-compartment model with 1st order absorption and 1st order elimination optimally describes the analyzed data. Parameter estimates of ka (0.077 h-1 [9%], typical value [relative standard error]), V (32.9 L 70kg-1 [37%]) and CL (22 L h-1 [8%]) show good predictive ability. Significant covariate effects include total bodyweight on elimination clearance and distribution volume and eGFR on elimination clearance. The effects of eGFR on the elimination clearance are optimally described by a power law parametrization centered around 105 mL/min/1.73m2. Estimated population elimination clearance equals 23.12 L/h/70kg and distribution volume equals 32.91 L/70kg.
Conclusion: Lisinopril dose and regimen adjustments for paediatric patients should include eGFR on top of weight adjustments. Extending population pharmacokinetic modelling with a Bayesian approach to other therapeutics can contribute to informed dosing in renally impaired children.

Hypertension

P1-129 - Change in obesity prevalence among youth referred for hypertension: interim analysis of The Study of the Epidemiology of Pediatric Hypertension (SUPERHERO) Registry

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Background: Hypertension is a leading risk factor for cardiovascular disease and, in youth, increases cardiovascular risk. However, critical knowledge gaps remain in our understanding of risk factors for target organ damage and treatment response in youth, including the true nature of obesity as a risk factor.
Objective: To determine longitudinal changes in the prevalence of obesity among youth referred for subspecialty evaluation of hypertension across heterogeneous healthcare systems.
Design/Methods: The Study of the Epidemiology of Pediatric Hypertension (SUPERHERO) Registry is an ongoing multicenter retrospective cohort of youth referred to subspecialty care for hypertension disorders in North America. Inclusion criteria are initial visit for hypertension disorder (by ICD-10 codes) from 1/1/2016–12/31/2021 and age <19 years. Exclusion criteria are pregnancy, kidney failure on dialysis, or kidney transplant. Data obtained via validated bioinformatics methods and include demographics, anthropometrics, and blood pressure, and for this analysis we excluded participants <2 years of age and those missing data. Weight category was classified according to Centers for Disease Control definitions for overweight and obesity. We tested for trends across year using linear regression and Jonckheere-Terpstra, Cochran-Armitage trend, and Cochran-Mantel-Haenszel tests.
Results: Of 3,384 participants, median age was 14.3 years [IQR 10.5–16.4], 37% were female, 29% identified as Black/African American, 17% identified as Hispanic/Latino, and 64% had public insurance. We observed a significantly increased proportion of obesity and more severe obesity across time (Figure 1).

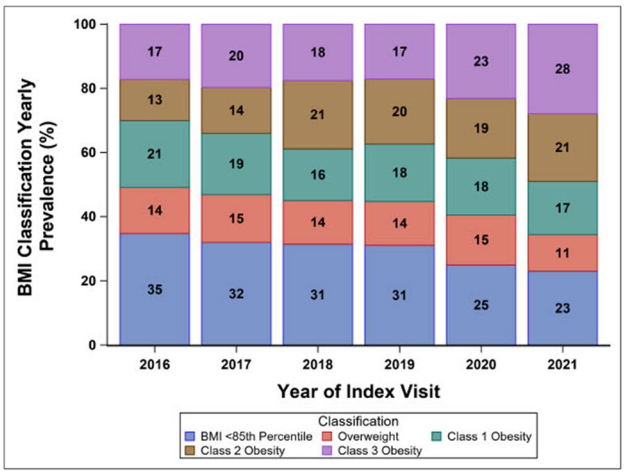

Figure 1. Increased prevalence of obesity over time in the SUPERHERO Registry.

Conclusions: The SUPERHERO Registry uses rigorous bioinformatics methods to collect electronic health record data to define pediatric hypertension disorder epidemiology and close key knowledge gaps. In this interim analysis, obesity increased in prevalence over time. Ongoing analyses are investigating why we observed these patterns including the impact of health disparities such as food insecurity and healthcare coverage.

Hypertension

P1-130 - Short term blood pressure variability in childhood-onset systemic lupus erythematosus (cSLE)

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Introduction: Hypertension (HTN) in cSLE is a modifiable factor in decreasing cardiovascular events and largely depends on mean-BP values. It is known that nighttime-BP dipping is attenuated in SLE. In adults +/- SLE, BPV is predictive of adverse cardiovascular events. We aimed to assess short-term BPV among cSLE patients +/- HTN using 24-hr ambulatory blood pressure monitoring (ABPM).
Methods: ABPM results for 58 cSLE patients were compared to 58 non-SLE controls from HTN clinic: propensity-score matched for age, gender, bmi z- score, ethnicity and race. Short-term BPV indices for daytime, nighttime and 24-hrs were calculated using : standard deviation(SD), average real variability(ARV), coefficient of variation(COV), and 24-hr weighted standard deviation(wSD). We assessed association between BPV and demographic, biochemical, disease activity score (Systemic-Lupus-Erythematosus-Disease-Activity-Index), current and cumulative steroid dosing (for past 12 months) normalized for weight.
Results: Of cSLE patients (median-age of 15.5 (14.4,17.0), 76% were female, and 31% were hypertensive. Median-BPV indices were lower in cSLE patients than matched controls reaching statistical significance in 24-hr systolic SD, COV ARV, and wSD, daytime systolic SD, and nighttime diastolic ARV (see Table-1). By subset analysis the same pattern was true for hypertensive and normotensive patients. Differences in wSD argue against attenuated dipping causing lower BPV. There was no significant correlation between BPV and C3 or DSDNA levels or disease activity score. However, there were negative correlations for cumulative steroid dose with 24-hr systolic SD(r=-0.31), COV(r=-0.35) and systolic wSD(r=-0.29). Current steroid dose was also negatively correlated with 24-hr systolic(r=-0.31) diastolic SD(r=-0.32), 24-hr systolic COV(r=-0.32) and daytime diastolic COV(-0.37).

Table-1 showing Median BPV indices in SLE patients compared to non-SLE controls using Mann Whitney U

			SLE=58	Non-SLE
Standard Deviation (SD)	Systolic	24-hr	**10.2***	**12.4**
		Daytime	**9.27***	**10.5**
		Night-time	**8.02***	**8.73**
	Diastolic	24-hr	**9.99***	**11.59**
		Daytime	8.89	9.73
		Night-time	7.55	7.71
Average Real Variability (ARV)	Systolic	24-hr	**8.15***	**9.17**
		Daytime	**8.09***	**9.57**
		Night-time	**7.06***	**8.62**
	Diastolic	24-hr	7.85	8.03
		Daytime	7.77	8.54
		Night-time	6.30	7.16
Coefficient Of Variance (COV)	Systolic	24-hr	**9.16***	**10.82**
		Daytime	8.19	8.39
		Night-time	11.6	12.6
	Diastolic	24-hr	**14***	**16.3**
		Daytime	12.3	12.6
		Night-time	11.6	12.5
Weighted Standard Deviation (wSD)	Systolic	NA	**9.07**	**10.15***
	Diastolic	NA	8.60	9.38

* Denotes p value < 0.05, Abbreviations BPV: Blood pressure variability, SLE: Systemic Lupus Erythematosus

Conclusion: Several BPV indices were lower in cSLE subjects than non-SLE controls, regardless of whether they are hypertensive or normotensive. Steroid exposure was negatively correlated with several of BPV indices. The significance of this correlation and the lower BPV indices in cSLE patients has to be explored in future studies.

Hypertension

P1-133 - Refractory Hypertension Secondary to Mercury Intoxication

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Background: Mercury based thermometers have been in use since the early 1700s, becoming the gold standard for measuring core temperature. Given mercury's known toxicity, current recommendations discourage their use, although mercury thermometers can still be found. We present a case of severe refractory hypertension and electrolyte derangements due to a mercury exposure from a broken thermometer.
Observation: We present a case of a previously healthy 11-year-old female who initially presented with myalgias/arthralgia's, headache, agitation and palmar desquamation. Nephrology was consulted for elevated blood pressures that ranged from 130s-150s/110s-130s. She underwent an extensive evaluation for secondary hypertension. Plasma metanephrine and normetanephrine levels were elevated at 0.28 nmol/L (reference value: <0.5 nmol/L) and 2.6nmol/L (reference value: <0.9 nmol/L) respectively. Cortisol, thyroxine, renin, aldosterone levels were normal. ^{131}I-MIBG scintigraphy failed to demonstrate Pheochromocytoma. Further history revealed that in June of that year she and other children played with a broken mercury-based thermometer, resulting in the heavy metal exposure. Elevated levels of mercury were observed in both blood and urine: 38 ng/mL (reference value: < 10 ng/mL) and 58 mcg/24H respectively. She was treated with four anti-hypertensives (Amlodipine, Labetalol, Doxazosin and Clonidine). IV chelation therapy with 2,3-dimercapto-1-propanesulfonic acid improved the mercury levels and over time the anti-hypertensives were able to be weaned off completely.
Key message: Mercury Intoxication can present as resistant hypertension, mimicking a pheochromocytoma. Anticipatory guidance by Pediatricians should include not only promoting the use of digital thermometers only but also removing mercury-based technologies such as thermometers and sphygmomanometers from the home.

Transplantation (including CMV, EBV & BK infections)

P1-134 - Agreement of the CKiD Under 25 (U25) equation with measured glomerular filtration rate in pediatric solid organ transplant recipients

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Background: Equations for estimated GFR (eGFR) are a commonly used alternative to assess kidney function easily in clinic and to guide clinical practice. We aimed to test the accuracy of a newer estimating equation, CKiD Under 25 (U25) eGFR with measured nuclear GFR (mGFR), compared to the previously validated Modified Schwartz equation in a single-centre cohort of pediatric solid organ transplant recipients.
Methods: In a pediatric cross-sectional study of solid organ transplant recipients ages 0-18 years at the Hospital for Sick Children, transplanted from January 2000 to June 2016, we compared the creatinine-based U25 eGFR with at least one (diethylenetriamine pentaacetate) DTPA-measured GFR (mGFR) post-transplantation. Using Bland-Altman analysis, we tested accuracy, precision, and bias between log-transformed mGFR and log- transformed CKiD U25-determined eGFRs, and compared them to the Schwartz equation.
Results: Among 1109 children, 58% were male, mean age was 7.4 years (standard deviation of 5.3), and 87% had a mGFR ≥ 60 ml/min/1.73m^2. Organ transplanted was 44% kidney, 25% liver, 25% heart, 5.1% lung, and 1.3% small bowel and multiple organ recipients. Modified Schwartz had a bias (mean difference) of 0.22 (95% CI 0.19, 0.24) and root-mean-square error (RMSE) of 0.41; 97% of the data was within the 30% limit of accuracy and 44% within 10%. The CKiD U25 equation had a bias of 0.23 (95% CI 0.20, 0.25) and an RMSE of 0.44; 94% of the data was within the 30% limit of accuracy and 41% within 10%.
Conclusion: Both estimating equations performed well in pediatric solid organ transplant recipients and the modified Schwartz performed marginally better when compared to CKiD U25 equation. Both equations could be clinically, although the simplicity of using the bedside Schwartz equation allows for widespread use worldwide.

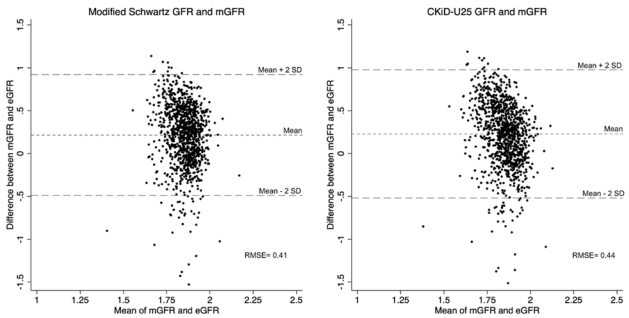

Figure 1. Comparison of the Bland-Altman plot agreement between the eGFR by CKiD U25 equation and the Schwartz bedside equation with the mGFR

Transplantation (including CMV, EBV & BK infections)

P1-135 - Effect of CYP3A5 genotype-guided versus conventional initial dose of tacrolimus in children with kidney transplants

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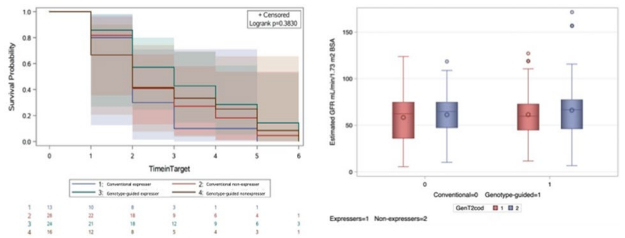
Background: *CYP3A5* tacrolimus polymorphisms predict its metabolization. We aimed to test the advantage of a genotype-guided starting dose after kidney transplantation to reduce the time to target drug levels and improve allograft surveillance.
Methods: We performed a single-center, open-label parallel group, randomized controlled trial in kidney recipients (0-18 y/o) at the

Hospital Infantil de México, Federico Gómez, from Jan-2013 to Dec-2018. Patients were assigned to one of two groups. The genotype-guided group received the dose according to the *CYP3A5* polymorphisms (*AA1*1, AG1*3* [expressers], and *GG3*3*, [non-expressers]). The conventional-dose group received the standard of care. We followed them for 12 months registering time to target levels, estimated glomerular filtration rate (eGFR), rejection, and nephrotoxic events.
Results: We included 81 patients; 40 received the genotype-guided dose, the mean age at transplantation was 13.3 y/o, 51.8% were female. There was a higher frequency of expressers in the genotype-guided than the conventional-dose group (29.6 Vs 16.1% p=0.04), having a higher number of *AA1*1*. There were no differences in the time to achieve levels within-target (8-10 ng/L) *logrank=0.182* between groups. There were no associations with rejection, OR 0.86 (95% CI 0.26-2.84, SE 0.606), or nephrotoxicity events, OR 5.85 (95% CI 0.60-56.8, SE 1.161) and the intervention. The eGFR remained similar (63.1 27.4 Vs 60.3 22.3 mL/min/1.73 m2 SC p=0.32) among groups. The subgroup analysis by genotype showed that expressers in the genotype-guided dose group took longer to achieve target levels (5 vs 3.2 mean weeks, *log-rank= 0.383*) (Figure)
Conclusions: Tacrolimus *CYP3A5* genotype-guided initial dose after kidney transplantation did not show benefits on time to target levels, rejection, tac related nephrotoxic events or eGFR after a 12-months follow-up in our cohort. The higher frequency of expressers in the genotype-guided group could influence the results, showing a high impact of the polymorphisms. New dosing strategies are needed to improve accuracy.

Figure. Left panel, time to tac within target trough levels (8-10 ng/L). Right panel, eGFR after 12 months of follow up by intervention and genotype group



**Survival analysis with Bonferroni adjustment. Cuantitative analysis using two way ANOVA*
Tac: tacrolimus, eGFR: Estimated glomerular filtration rate

Transplantation (including CMV, EBV & BK infections)

P1-136 - Influence of tacrolimus CYP3A5 polymorphisms on the dose-level response after pediatric kidney transplantation

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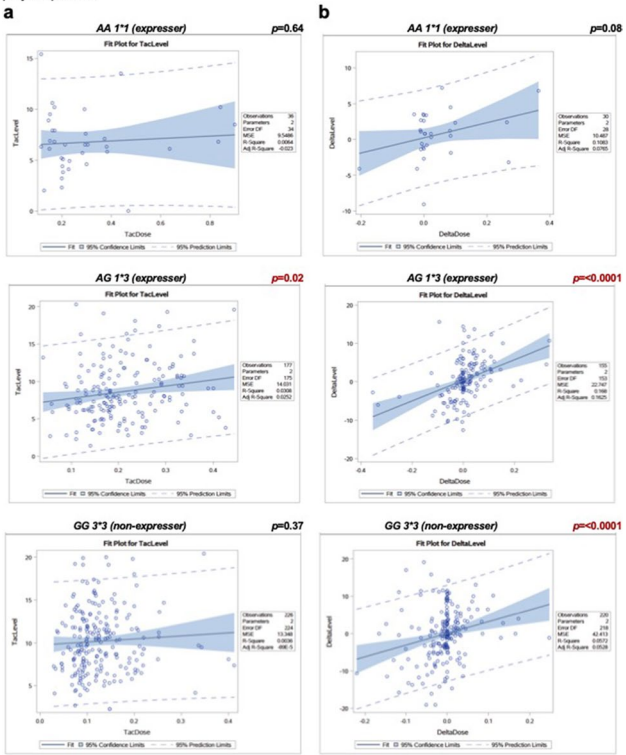
Background: Tacrolimus exhibits wide inter and intra-patient variability. *CYP3A5* tacrolimus polymorphisms predict its metabolization. We aim to identify the influence of *CYP3A5* allelic variants on the tacrolimus pharmacological parameters in an assignation-dose genotype-guided trial.
Methods: We performed an exploratory data analysis of pharmacological parameters from a single-center, non-randomized, open-label clinical trial in children from 0-to 18 years of age who received a kidney transplant at our institution from January 2013 to December 2018. All subjects were genotyped before transplantation and assigned to one of two groups: the Genotype-guided group, which initial dose was according to the *CYP3A5* polymorphisms and the Conventional-dose group (see abstract IPNA22-0542), with further dose adjustments in the decision of the clinicians. We followed them for six weeks, recorded the prescribed tacrolimus dose and trough level, and calculated the deltas between time points.
Results: We included 81 subjects; 40 received the genotype-guided dose, the mean age at transplantation was 13.3 y/o, 51.8% were female. The linear regressions showed no association between tacrolimus dose and levels in the genotype-guided dose group (r^2=0.0003, p=0.78) or the conventional-dose group (r^2=0.0008, p=67). However, both groups had a linear association between delta-dose and delta levels (r^2=0.138, p=<0.0001 and r^2=0.081, p=<0.0001, respectively). The subgroup analysis by genotype showed an r^2=0.168, p=<0.001 between the delta-dose and delta level for the *AG1*3*allele. This group reached statistical significance for the dose and trough levels achieved (r^2=0.0308, p= 0.02). For the *GG3*3* polymorphism was only significant in the delta analysis (r^2=0.057, p=<0.001), while the *AA1*1* alleles did not show any associations between dose vs trough level or deltas (r^2=0.006, p=0.64 and r^2=0.108, p=0.08 respectively) (Figure)
Conclusion: The delta-dose and delta-level translate the clinician's decisions. The trough levels' response to dose adjustments might be guided by the *CYP3A5* genotypes, specifically the *AG1*3*. Further studies are needed to estimate more accurate associations.

Figure. Linear regressions of the first six weeks after transplantation of the tacrolimus trough level vs dose (panel a) and the tacrolimus delta-levels vs delta-dose (panel b) across the different CYP3A5 polymorphisms



Transplantation (including CMV, EBV & BK infections)

P1-137 - Twelve-year-old female with abdominal tuberculosis five years after renal transplant at Instituto Nacional de Pediatría, Mexico City

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Pediatric posttransplant infectious complications secondary to immunosuppression have been emerging. Extra pulmonary tuberculosis cases in the pediatric population have not been published yet. Death was the common outcome in two adult cases reviewed in literature.
We present the case of a twelve-year-old female with history of living-donor kidney transplant in 2017. Immunosuppression with tacrolimus, mycophenolate mofetil and prednisone was present. Patient attended the emergency room with fever, abdominal pain, vomiting and diarrhea. Symptoms disappeared; fever persisted despite broad spectrum antibiotics. Approach as fever of unknown origin (FUO) was followed. QuantiFERON was negative. Positron emission tomography (PET) scan reported hypermetabolic activity in cervical and retroperitoneal lymph nodes and bone narrow. B-cell lymphoma was considered as differential diagnosis. A cervical lymph node biopsy was performed. Histopathologic report was negative for malignant or tumoral cells, chronic granulomatous lymphadenitis with caseating and suppurative granulomas with giant cells were found. Antituberculosis treatment with isoniazid, rifampin, ethambutol, and pyrazinamide was initiated. Fever persisted. Fungal lesions were observed in abdominal ultrasonography. Abdominal magnetic resonance imaging (MRI) demonstrated an heterogenous lymph node mass 56mm x 57mm with an adjacent encapsulated, hypointense image 25mm x 27mm A retroperitoneal biopsy was programmed. A caseous lymph node with whitish matter and adhesions to appendix, terminal ileum, ascendent colon and epiploon was observed. Necrotic mesenteric tissue was removed and because a perforation at ileum was found, an ileostomy was performed. PCR for Mycobacterium tuberculosis from intestine tissue and lymph node were positive. Enterococcus faecium and Klebsiella pneumoniae was isolated from peritoneal fluid culture. Doble therapy with meropenem and linezolid for 14 days was indicated, fever ceased. Patient was successfully discharged with antituberculosis drugs.
Keywords: renal transplant, extrapulmonary tuberculosis, fever of unknown origin

Transplantation (including CMV, EBV & BK infections)

P1-139 - Comparison of graft survival after pediatric kidney transplantation from living and deceased donors: 2007-2018 French cohort

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Objectives: It is usually recognized that living donor (LD) kidney transplantation (KT) has better long-term results than deceased donor (DD) KT. We compared graft survival according to the type of donor (DD or LD) in the most recent French pediatric cohort.
Methods: We included all pediatric patients who received a first isolated KT in France between 2007 and 2018. The primary endpoint was graft survival at 5 years. We also described and compared the duration of dialysis, causes of kidney failure, HLA, EBV and CMV matching, donor characteristics and ischemia times in the 2 groups (mean±SD).
Results: 852 and 191 patients were included in the DD and the LD groups, respectively. The age at transplantation was slightly lower in DD group: 11.1±5.0 vs 12.0±4.4 years (p=0.01). The 5-year renal graft survival was 89% (CI95%: 87-91) and 89% (CI95%: 83-93%) in the DD and LD groups (p=0.678), respectively. Similar results with death censoring were observed: 90% (CI95%: 88-92%) versus 91% (CI95%: 85-94%). In the LD group, there were more preemptive transplants (52.2 vs 23.6%, p<0.01), but the same duration in dialysis before KT among dialyzed patients (18.9±25.1 vs 19.2±19.6 months, p=0.94), a shorter waiting time (6.5±6.8 vs 10.5±10.5 months) (p<0.01), shorter cold (3.3±2.9 vs 15.9±5.1 hours) and warm ischemia times (48±24 vs 54±36 minutes) (p<0.01 and p=0.01), older donor (42.4±6.9 vs 15.2±7.7 years) (p<0.01) and better HLA matching (mismatches A: 0.8 vs 1.2, B: 0.9 vs 1.4, DR: 0.7 vs 0.8 and DQ: 0.6 vs 0.7 (p<0.01).
Conclusion: The 5-year graft survival is currently the same between DD and LD in the most recent French pediatric cohort. The next step is to compare these results with the 1995-2006 pediatric cohort to analyze factors associated with graft loss in both groups and in both cohorts.

Transplantation (including CMV, EBV & BK infections)

P1-141 - Ebstein-Barr virus-associated smooth muscle tumor in a boy after kidney transplantation

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Introduction: Epstein-Barr virus (EBV) has been implicated in the etiology of a wide range of malignancies. Certain EBV-driven neoplasms, such as smooth muscle tumors (SMTs), manifest typically in immunocompromised patients. We present a case of multiple EBV-related SMTs in a boy after kidney transplantation.
Case report: a male neonate presented immediately after birth with impaired kidney function, reflected in elevated blood urea nitrogen (BUN) and creatinine levels. He was born after an uneventful pregnancy to nonconsanguineous caucasian parents. Ultrasonography revealed bilateral dysplastic kidneys. His kidney function deteriorated, and at the age of 10 months, peritoneal dialysis was started. Three years later, he received a deceased donor's kidney with immediate graft function. Initial immunosuppression (IS) was achieved with interleukin-2 receptor blocking induction, followed by methylprednisolone, mycophenolate mofetil (MMF), and tacrolimus. Two months later, a primary EBV infection triggered the onset of post-transplant lymphoproliferative disease (PLTD). He received six cycles of rituximab. MMF was discontinued, and tacrolimus switched to everolimus. This resulted in complete PTLD remission. However, two years after the last dose of rituximab, multiple round inhomogeneously hypoechoic liver and spleen mass lesions materialized on routine ultrasound scans. PET-CT and fine-needle biopsy did not provide additional information. We decided on a close sonographic follow-up due to good clinical condition. Six months later he developed severe BK-virus nephropathy. Additional IS reduction and, eventually, complete weaning of IS was unsuccessful and resulted in a lethal systemic BK-virus infection. Post-mortem findings revealed multiple EBV-associated SMTs in the liver, spleen, and caecum. The lesions were mostly composed of spindle-cells with eosinophilic cytoplasm and elongated nuclei. In-situ hybridisation was EBV positive in 20-30% of tumor-cell nuclei.
Conclusion: The occurrence of SMTs should be considered in pediatric kidney transplant recipients with EBV infection and round sonographic lesions in different organs, particularly in the liver, spleen, and lungs.

Transplantation (including CMV, EBV & BK infections)

P1-142 - Prednisolone pharmacokinetics after oral prednisone administration in pediatric patients with kidney transplant

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Background: Glucocorticoids are one of the primary treatments for pediatric kidney transplantation. Dosages remain empirically established while therapeutic drug monitoring could be relevant in terms of efficacy and tolerance. Goals for this study were: 1) to build a population pharmacokinetics (PPK) model of free prednisolone, prednisone active form, in pediatric kidney transplant recipients; 2) to identify covariates accounting for interindividual variability (IIV) of PK parameters; 3) to investigate drug exposure-tolerance relationships.
Methods: 97 samples were obtained from 39 pediatric kidney transplant recipients (aged 3.4 to 17.2 years) in order to investigate prednisone PPK. We selected children receiving oral prednisone as part of their immunosuppressive regimen. A PPK analysis was performed using Monolix.
Results: Large IIV was found as prednisolone was undetectable at H12 for some patients but not at H24 for others. Weight and cyclosporin co-treatment influenced pharmacokinetics. Free prednisolone clearance (CLu) and volume of distribution scaled allometrically for 70 kg were respectively 27.6 L/h and 101 L. Cyclosporin co-treatment decreased CLu by 67%. High blood pressure and new onset diabetes after transplant were associated with free daily prednisolone exposure.
Conclusion: This study is the first prednisolone PPK analysis in kidney-transplanted children. Some of the IIV in PK parameters was explained by weight and cyclosporine co-treatment. These data suggest that dosages must be adapted after identifying variability factors to optimize efficiency and limit side effects. A therapeutic drug monitoring in kidney-transplanted children to adjust the dosages may be useful, especially regarding tolerance issues.

Transplantation (including CMV, EBV & BK infections)

P1-143 - SARS-CoV-2 infection in pediatric kidney transplant recipients in the first year of the pandemic

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[5]*Hospital El Cruce, Pediatric Image, Florencio Varela- Buenos Aires, Argentina*
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Description: Case 1: 17-year-old femele. Hypertensive, obese and hypothyroid. Deceased donor kidney transplantation (DDKT). Five months after transplantation (TX), she developed acute cellular rejection and received MP and TMG. DSA negative. Cough and fever 9 months after TX. Positive SARS-CoV-2 PCR test. Lymphopenia since admission; clinical and radiological deterioration; multisystem inflammatory parameters; viral and bacterial coinfections; convulsions; mechanical ventilation; KRT. Convalescent plasma administration; abrupt deterioration, dying 48 days after admission. **Case 2:** 16-year-old male. DDKT. Four months after TX: borderline acute cellular rejection, MP administration. One year after TX, IA acute cellular rejection. Administration of 3 MP pulses, and TMG. Upon admission, fever was detected, positive COVID-19 test. Leukopenia, no cough, but compromised lung parenchyma on X-rays. Convalescent plasma administration. Clinical improvement. Discharge after 13 days. After COVID-19 infection, he developed increased creatinine levels, confirming IB acute cellular rejection. **Case 3:** 8-year-old female. DDKT. Favorable evolution. Eighteen months after TX, she tested positive for SARS-CoV-2 (PCR). Subsequent diarrhea and cough. No radiological compromise. Discharged with a Cr level of 0.7 mg/dl. She was followed up 14 days

later, with a Cr 1.6 mg/dl, T cell-mediated rejection, Category 4 of the Banff, Type IB. MP administration. **Case 4:** 19-year-old male. Transplanted twice: at 8 years old, DDKT with immediate graft thrombosis and transplantectomy. Second DDKT at 15 years old, with a favorable evolution and graft function until June, 2019, when he developed TMA and was treated with Eculizumab, evolving favorably. Cr: 1.3 mg/dl, Proteinuria: <500 mg/day. Normotensive, without acute rejection. DSA negative. He was admitted for Eculizumab infusion following a SARS-CoV-2 PCR test; infusion proceeded without complications. The SARS-CoV-2 PCR test was positive. He was admitted without symptoms and subsequently developed a cough; no respiratory distress or fever. Compromised lung parenchyma on X-rays. Slight increase in Cr: 1.58 mg/dl.

Transplantation (including CMV, EBV & BK infections)

P1-144 - Pancreatic Pseudocyst in a Post Kidney Transplant Child

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Introduction: Acute pancreatitis is a rare complication after kidney transplantation. Pancreatic pseudocysts regardless of etiology has a low incidence rate. Both are extremely rare in the pediatric population. We report a case of a 13-year-old child who presented with both. She developed acute pancreatitis post-transplant and subsequently developed a pancreatic pseudocyst. The size and accompanying symptoms pointed to a surgical management, however this case resolved spontaneously without drainage.
Case Presentation: A 13 year old girl diagnosed with FSGS 9 months prior, underwent kidney transplantation(KT) from living-non-related-donor, with rATG induction, and tacrolimus, MMF, steroids as maintenance. Developed epigastric pain after 21 days. Work-ups showed elevated amylase and lipase. Managed as acute pancreatitis. Ultrasound showed fluid collection likely from pancreatic secretion, which was drained.Pain resolved.
Epigastric pain recurred after two months. Ultrasound showed no loculated fluid. Pain resolved with pain medications. Third month post-KT abdominal pain recurred. Elevated amylase and lipase with pancreatic tail thick-walled complex fluid collection(pseudocyst) was noted, Parenteral nutrition, octreotide and pancreatin were started with no improvement. Increase in pseudocyst size was noted on serial monitoring to a volume of 200cc(Fig1),pain became intolerable. Fentanyl drip,celiac plexus block, and sedatives all afforded minimal relief. Parents consented to surgical removal but was advised to wait 1 week due to intermediate wall-thickness.
While waiting, pain intensity decreased, ultrasound revealed decreased pseudocyst volume from 200cc to 168cc. Pain continued to decrease in intensity, surgery was put on hold. After another 10days, pseudocyst volume decreased to 20cc. Amylase and lipase levels returned to normal, and pain resolved with no recurrence. Ultrasound after 1 month showed normal pancreas with no pseudocyst.
Conclusion: Prompt evaluation for pancreatitis should be done for patients presenting with abdominal pain after kidney transplantation. Pancreatic pseudocyst is rare in children but potentially troublesome. Skillful assessment and appropriate management are important to avoid potentially serious complications.

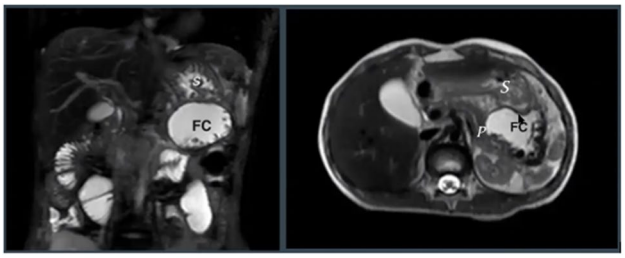

Figure 1. Upper Abdomen MRI. FC-Fluid Collection, P-pancreas, S-stomach

Transplantation (including CMV, EBV & BK infections)

P1-145 - Influence of migration status on practice and clinical course of pediatric kidney transplantation

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Objectives: to investigate the incidence trend of transplanted immigrant children and to analyze kidney transplant (KTx) practice and outcome for immigrant compared to native children.
Methods: We performed a retrospective study: 1. to analyze the percentage trend of "foreign patients" (FP) (children with one/both parents born in non-Western European countries) aged ≤21 years, transplanted in the period 2002-2021 at our Center; 2. to compare data of FP and "domestic patients" (DP) during the period 2017-2021.
Results: The percentage of FP was 22.3% and 34.6% (p:0.04) in the decades 2002-2011 and 2012-2021 respectively. Baseline and transplantation characteristics of patients in the period 2017-2021 are summarized in Table 1.

Table 1: Baseline and transplantation characteristics

	Total n = 75	Domestic patients n=50	Foreign patients n=25	*p*
Age at transplantation (years) [a]	14.1 (10.6-16.7)	14.6 (11.4-16.8)	13.7 (10.1-15.6)	0.18[d]
Sex: female, *n* (%)	26 (34.7)	14 (28.0)	12 (48.0)	0.08[e]
Primary cause of ESRD, *n* (%):				
CAKUT	34 (45.3)	23 (46.0)	11 (44.0)	
Cystic kidney disease	12 (16.0)	11 (22.0)	1 (4.0)	
FSGS	4 (5.3)	3 (6.0)	1 (4.0)	
Other glomerular disease	5 (6.7)	4 (8.0)	1 (4.0)	
CNS	3 (4.0)	0	3 (12.0)	
Hemolytic uremic syndrome	4 (5.3)	3 (6.0)	1 (4.0)	
Hereditary nephropathy	5 (6.7)	3 (6.0)	2 (8.0)	
Kidney failure	6 (8.0)	1 (2.0)	5 (20.0)	
Others	2 (2.7)	2 (4.0)	0	
Follow-up time (months) [a b]	27.3 (14.6-47.0)	32.0 (17.5-49.2)	18.7 (6.4-39.9)	**0.04**[d]
Pre-emptive KTx, *n* (%)	25 (33.3)	22 (44.0)	3 (12.0)	**0.005**[e]
LD KTx, *n* (%)	19 (25.3)	18 (36.0)	1 (4.0)	**0.003**[e]
Time on dialysis before KTx (months) [a]	10.9 (0-23.7)	3.7 (0-15.9)	16.7 (8-30.9)	**0.002**[d]
HLA mismatches (A, B, DR) [c]	3.2 (±1.0)	3.0 (±1.0)	3.6 (±1.0)	**0.01**[f]
> 1 mismatch on DR, *n* (%)	6.0 (8.0)	4.0 (8.0)	2 (8.0)	ns

[a]Data are presented as median and interquartile range
[b]Follow-up time was calculated per patient in months from the KTx date until the first ARE or KTx failure or the last follow-up visit
[c]Data are presented as mean ± standard deviation
[d]Mann–Whitney U-test
[e]chi-square test
[f]t-Test for unpaired data

Compared to DP, FP receive less pre-emptive and living donor (LD) KTx and spend more time on dialysis before KTx. Moreover, Kaplan-Meier survival analysis was used to assess the 5-year KTx survival (patients censored at acute rejection episodes, ARE) and showed a significant increased risk of ARE in FP compared to DP (7 vs 1 events, $p < 0.003$). The first ARE occurred after a period of 3.8 months (IQR 3.1-7.2) and 26.1 months in FP and DP patients respectively. We also found a significant difference in HLA mismatch with a higher mean value in FP population.
Conclusion: Our study confirms the progressive increase of FP in recent years in Italy. In line with other studies in Europe, we found disparities in practice and outcomes of KTx in FP, that can be attributed to cultural factors and language difficulties, even if immunological and genetic factors, such as different pharmacokinetic profile, should be analyzed. While waiting to better understand the mechanisms behind this phenomenon, it can be useful to build a multidisciplinary network and ad hoc initiatives around FP, in order to support these patients and their family to improve their outcome.

Transplantation (including CMV, EBV & BK infections)

P1-146 - Humoral response to COVID-19 mRNA vaccines in a cohort of young kidney transplant recipients from a single Center in Northern Italy

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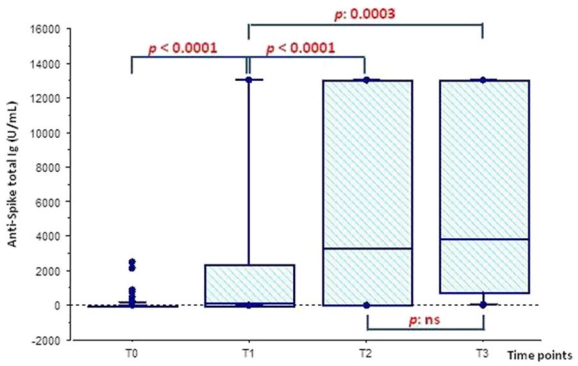
Objectives: To investigate immune-response to COVID-19 vaccines in young kidney transplant (KT) recipients from Northern Italy.
Methods: We prospectively studied KT patients aged 12-25 years, managed in our Center on maintenance IS therapy (corticosteroids, CNI and anti-proliferative agents), eligible for antiSARS-Cov2 vaccination according to the schedule of the Italian Medicines Agency for immunosuppressed patients (two doses plus additional dose one month later). From 1st July 2021 to 28th February 2022 we evaluated antiSpike-protein antibody response at T_0 (before vaccine), T_1, T_2 and T_3 (14±3 days after 2nd and 3rd dose and 90±7 days after 3rd dose, respectively) to BNT162b2 (Pfizer/BioNTech) or mRNA-1273 (Moderna). AntiSpike total Ig titer cut-off was 0.8 U/ml (Roche® Elecsys Anti-SARS-CoV-2-S). Exclusion criteria: KT or additional IS within 6 months, relapse of primary disease, vaccine before KT, ongoing COVID-19, patients resident outside the Region.
Results: Eighty-seven patients were eligible; 68 patients were enrolled. Median age: 19.5 (IQR:16.3-21.9) years; median time from KT: 61.4 (IQR: 36.7-111.7) months. Five patients dropped out of study after enrollment.
Anti-SARS-Cov2 Spike Antibodies response to mRNA vaccines is shown in Figure1; 90% of non-responders at T1 (20 patients) seroconverted at T3.

Figure 1: Anti-SARS-Cov2 Spike Antibodies response to mRNA vaccines



	T0	T1	T2	T3
Patients N.	66	55	51	42
Seroconverted pts N (%)	14 (21.2)	35 (63.6)	46 (90.2)	41 (97.6)
Ab titer (IQR)	0	188.0 (0-2408.7)	3374.0 (58.6-13000)	3905.5 (801.0-13000)

We didn't find correlation between time from KT (the shorter time, the most intensive immunosuppression) and Ig-titer. Twelve out of 58 pts developed COVID19 after the third additional vaccine dose; in this population AntiSpike Ig titer at T2 was lower compared to the value of non infected patients, even if not statistically significant: 144 U/ml (IQR:9.4-3683) vs. 4771 U/ml (IQR:79.1-13000) respectively. None patient had side effects, including acute rejection episodes or de novo DSA development.
Conclusions: KT pediatric recipients exhibit a satisfactory response after 2 doses of vaccine, that become comparable to that of immunocompetent population after the third. Furthermore, the response after two doses is better if compared with adult KT population (63.6% vs 4-48%).

Transplantation (including CMV, EBV & BK infections)

P1-147 - clinical characteristics and spectrum of BK viru replication after pediatric kidney transplantation: a single center experience

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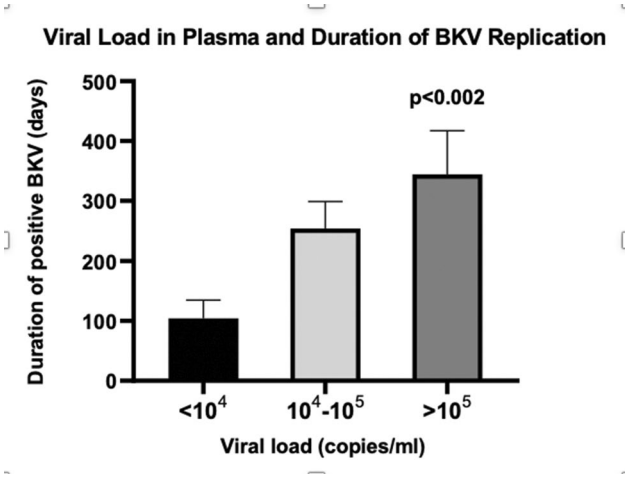
Background: BK virus (BKV) is a significant cause of acute and chronic kidney injury in kidney transplant recipients resulting in allograft loss. There is no standardized approach to monitoring and management of BKV after pediatric kidney transplantation.
Objective: The primary objective of the study was to determine the incidence of BKV replication among kidney transplant recipients.The secondary objective was to identify risk factors that predict the more severe phenotype of BKVAN and describe therapeutic approaches.
Methodology: We conducted a retrospective case-control study of pediatric kidney transplant recipients <21 years of age transplanted between 2014 and 2020. Categorical variables were compared between BKV and non BKV groups by chi-square analysis, and continuous variables were compared by student t test. The magnitude of peak viral load was categorized, and duration of viral replication was compared by ANOVA.
Results: Of 117 patients, 41 (35%) had BKV replication. The BKV group had more African-American recipients and were more likely to

have a CMV serologic mismatch. Only 4 patients (10%) developed BKVAN. Patients with BKVAN had a higher peak viral load (595,537 ± 279,428 vs 32,724 ± 63,847 copies/ml, p <0.01) and a longer duration of BK viremia compared to the asymptomatic BKV replication group (413 ± 183 vs 169 ± 138 days p <0.01).



The first line of therapy was reduction in immunosuppression in 31 (76%). Leflunomide was used when immune suppression reduction did not decrease BK viremia in 10 (24%) and one patient received low dose cidofovir. Percent-rise in serum creatinine correlated with the intensity of viral load (p <0.02).

Conclusion: Patients with the highest viral loads and longest duration of viral replication are at risk for BKVAN. BKV replication may be a surrogate marker for excessive immune suppression. If managed early with reduction of immune suppression, morbidity from BKVAN can be mitigated.

Transplantation (including CMV, EBV & BK infections)

P1-148 - Lower Access to and poorer outcomes of Kidney Transplant in Aboriginal and Torres Strait Islander Children and Young Adults of Australia: Results from the ANZDATA registry.

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Introduction: Access to kidney transplant and transplant outcomes for Aboriginal and Torres Strait Islander Children and Young adults (ATCYA) of Australia have not been investigated in detail. We aim to describe if equitable patterns of transplant access and outcomes occurred among ATCYA and other children and young adults (OCYA) of Australia.

Methods: Participants were 3736 patients aged ≤24 years who started renal replacement therapy (RRT) in Australia between 1963-2020 using the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA). Primary outcomes were patient survival on RRT, time to first kidney transplant, patient's death and death-censored graft survivals among ATCYA, compared with OCYA. Cox proportional hazards model was applied to analyse the 5-year outcomes.

Results: During a median 8 years ((IQR 2.6-15) follow-up, 2762 (74%) children and young adults received kidney transplantation (93 were ATCYA and 2669 OCYA). Median age at transplantation was 18 (IQR 12-22) years and did not differ significantly between groups. However, ATCYA were less likely to receive a transplant within 5 years (46.5% vs. 83%, HR=0.36, 95% CI 0.30-0.44, p<0.001), receive a living donor transplant (20.4 vs. 43.9%, p < 0.001) or receive pre-emptive transplantation (1.1% vs 13.6%, p < 0.001).

The overall five-year patient deaths on RRT were nearly 2-fold higher for ATCYA (17.4% vs 9.7%, p<0.001), however among transplanted patients, there was no difference in post-transplant mortality among the two groups (ATCYA vs. OCYA 8.6% vs 7.5%, p=0.7). ATCYA patients had higher five-year death censored graft failure (33.3% vs. 23.7%, p= 0.03).

Conclusions: During 1963-2020, ATCYA had lower access to kidney transplant, and poorer outcomes (indicated by higher 5-year patient's deaths on RRT and death censored graft failure) than OCYA. These findings emphasise the urgent need to define targeted strategies that improve access to kidney transplantation, and modify factors associated with discrepant graft survival post-transplant.

Transplantation (including CMV, EBV & BK infections)

P1-149 - Blood donor-derived cell free DNA (dd-cfDNA) as a non-invasive biomarker for BK polyomavirus-associated viremia and viruria.

Raja Dandamudi[1], Hongjie Gu[2], Charles Goss[2], Stuart Federman[3], Robert Woodward[3], Sham Dholakia[3], Leslie Walther[1], Vikas Dharnidharka[1]
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[3]*CareDx Inc, Medical Affairs, Brisbrane- CA, USA*

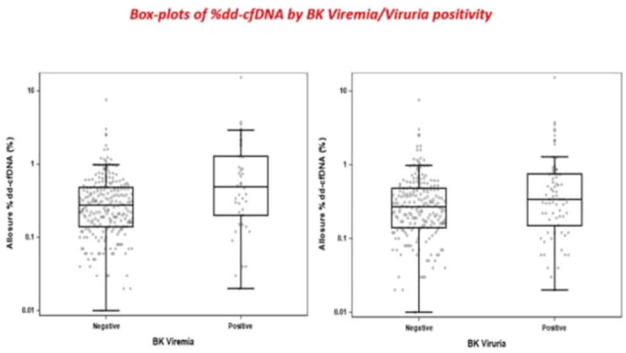
Background: Blood levels of dd-cfDNA elevate in various forms of kidney transplant injury, most notably used for detecting potential acute rejection.

Objective: We hypothesized that dd–cfDNA had a discriminating role between BK Viruria and Viremia and can act as a surrogate marker to quantify the severity of viral injury.

Design/Methods: We have performed longitudinal bio banking of plasma and urine in our PKTx population since 2013, combined with monthly testing for urine and blood BK virus DNA by PCR from months 1–12 post-transplant. In this study we assayed longitudinal bio banked and prospective plasma samples for dd–cfDNA levels (Allosure; CareDx) and associated to longitudinal BK viremia or viruria results. (positive defined as any detectable DNA). Statistical analyses were performed via SAS using least squares means mixed modeling.

Results: 274 simultaneously drawn plasma dd-cfDNA levels, plasma and urinary BK virus levels within the first-year post-transplant from 57 independent patients. Of the 274 samples we had 71 (25.9%) positive urinary samples and 42(15.32%) positive plasma samples. Patients with BK Viruria had a higher median dd-cfDNA of 0.34 (0.15-0.75) when compared with no BK viruria

0.27 (0.14-0.48).Patients with BK viremia had a higher median dd-cfDNA of 0.49 (0.20-1.28) when compared to with no BK viremia 0.28 (0.14-0.48). By longitudinal analysis (for within-subject variability), a significant rise of 0.88% in dd-cfDNA levels were seen at time of BK viremia (p = <0.0001). A lower but also significant rise of 0.49% in dd-cfDNA levels were seen at time of BK viruria (p = 0.003). There was a significant positive correlation between %dd-cfDNA and BK plasma viral load (correlation coefficient=0.21, p=0.0005),and significant positive correlation between %dd-cfDNA and BK urine viral load (correlation coefficient =0.17, p=0.004).



Conclusion(s): Our study proved the utility of dd-cfDNA to study the progression of BK virus reactivation in PKTx, and to track concomitant allograft injury.

Transplantation (including CMV, EBV & BK infections)

P1-150 - Anellovirus Dynamics prior to Acute Rejection (AR) or Major Infection Events (MIE) in Pediatric Kidney Transplant Recipients (PKTx).

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Background: Blood levels of non-pathogenic anellovirus (AnV) taxa have been postulated to represent a biomarker of the overall state of immunosuppression after transplantation. Prior studies, in adults, suggest that AnV levels rise with MIE and drop with AR.
Objective: The objective was to study the anellovirus trends with MIE and AR events in PKTx.
Design/Methods: In this study we assayed longitudinal biobanked and prospective serum samples for AnV DNA levels (copies/mL) and associated to standard of care monitoring and clinical results. To adjust for repeated measurements within subjects, we used a linear mixed model approach to test for differences in AnV DNA levels between complication groups (None, MIE at time of sample, AR at time of sample). A log transformation was used to better meet model assumptions, and results are reported on the log scale.
Results: 271 plasma samples from 46 children (Males 52%, white 83%, deceased donor 69%), as shown in Figure, most serum samples are positive for AnV through all time points. Mixed model results showed that the log AnV DNA (copies/mL) was elevated by 0.5 log for the MIE group (adjusted mean of 17.3 [95% CI, 16.1 to 18.4]) compared to the no complications group (adjusted mean of 16.8 [95% CI, 15.9 to 17.7]) (P=0.41). In contrast, results for the AR group showed a lowering of log AnV DNA (copies/mL) (14.3 [95% CI, 15.9 to 17.7]) by 2.5 log compared to the no complications group (P=0.12). Although neither result was statistically significant (likely due to small sample size), both results are consistent with the concept from cross-sectional studies of AnV load as an immunosuppression state biomarker.
Conclusion(s): In our PKTx cohort, our results suggest that longitudinal AnV levels seem to associate to AR and MIE events. Further prospective longitudinal testing in a larger multicenter cohort is recommended.

Transplantation (including CMV, EBV & BK infections)

P1-151 - Long-term results of kidney transplantation in children with bodyweight lower than 10 Kg.

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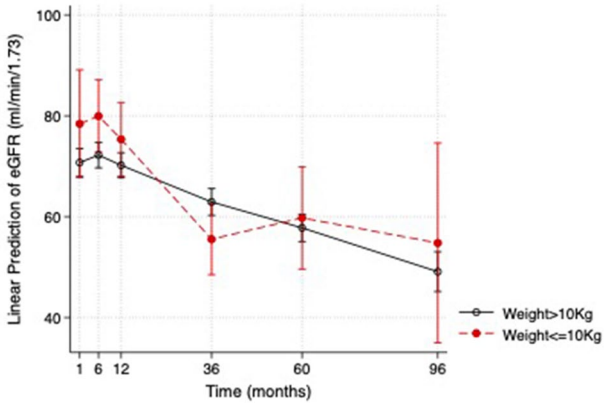
[2]*Hospital Samaritano de Sao Paulo, Pediatric Transplantation, São Paulo, Brazil*

Objective: To evaluate long-term results of kidney transplantation comparing low weight (<=10 Kg) to bigger children.
Methods: Unicentric cohort involving children who underwent kidney transplantation. The primary clinical outcomes were the 7 years death-censored graft survival, and the estimated glomerular filtration rate (eGFR) at 1, 3, 5, and 7 years. The main risk variable was weight at transplantation and children were categorized as G1: <= 10Kg and G2 > 10Kg. Covariables were CKD etiology, and kidney donor type (living/deceased). The survival estimates were fit through univariate and multivariable Cox regression models, and the eGFR over time was modeled using multilevel mixed-effects linear regression.
Results: The study involved 451 first kidney transplants in children (53 from G1 and G2 398 from G2), with a median age of 7.6 (4.0 to 12.5) years, 64% male, 53% CAKUT. G1 had a) more living related donors (28% versus 17%), and b) slightly different CKD etiologies, with more CAKUT (64% versus 52%) and hereditary diseases (23% versus 13%), both results tending towards a significant difference (p=0.06 in both cases). Graft survival at 7 years was 86% (75 to 99) in G1 and 84% (79 to 88) in G2 (p=0.791). The mixed-effects model revealed that both groups had a significant decline in eGFR over time (p<0.001), but with no significant difference (p=0.172) between groups (FIGURE 1). To adjust for the higher proportion of living donors in G1, we analyzed separately the subgroups according to kidney donor type, and these analyses did not change the results of the models.
Conclusions: The main finding of this study is the similar long-term results of kidney transplantation in both groups. This results in a sizeable number of low-weight children should uphold kidney transplantation in small children.

Transplantation (including CMV, EBV & BK infections)

FIGURE 1 – Estimated glomerular filtration rate over time in children according to weight at transplantation.



P1-152 - Comparing Serum Creatinine with Donor-derived Cell-free DNA (dd-cfDNA) as a marker of T Cell Mediated Rejection (TCMR) in Pediatric Kidney Transplant Patients

Raja Dandamudi[1], Stuart Federman[2], Robert Woodward[2], Sham Dholakia[2], Leslie Walther[3], Vikas Dharnidharka[3]
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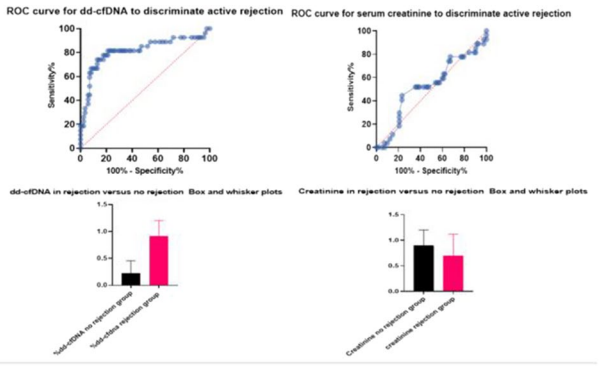
Purpose: TCMR is a major cause of kidney allograft failure which requires kidney biopsy for a definitive diagnosis. dd-cfDNA is an emerging biomarker used to assess kidney allograft injury, with scant pediatric data. This study was conducted to investigate the accuracy of dd-cfDNA as a marker of TCMR in a pediatric kidney transplant population.
Methods: In this retrospective single center observational study, we studied 54 patients who had concurrent 109 dd-cfDNA levels along with kidney biopsies within the first year post-transplant that showed either TCMR or normal, all other pathologies were excluded and we had no ABMR. We included both surveillance biopsies (3, 6 and 12 months) and diagnostic biopsies. We quantified dd-cfDNA by next generation sequencing using a targeted, multiplex PCR-based method for the analysis of single nucleotide polymorphisms (AlloSure, CareDx, Brisbane, CA). Treating each sample as independent, we divided the cohort into two groups (no evidence of TCMR vs Any TCMR, including subclinical rejection) and analyzed the data.
Results: The median (25-75 percentile) level of dd-cfDNA in patients with TCMR was significantly higher (0.91(0.54-1.2)) than in the no rejection group (0.22(0.14-0.45)) (P<0.0001) by Mann-Whitney U test. The area under the curve was 0.82 (95% CI, 0.71 to 0.93).At a 1% cutoff, of the dd-cfDNA had a 96% specificity (95% CI, 90% to 99%) and 33% sensitivity (95% CI, 19% to 52%) to discriminate active rejection from no rejection. Serum creatinine at time of biopsy did not discriminate active rejection from no active rejection. The median (25-75 percentile) level of creatinine in patients with active rejection was (0.70(0.53-1.1)) and was not statistically different from the comparison group (0.90(0.70-1.2)) (P 0.633). The area under the curve was 0.53.



Conclusions: This study supports the use of %dd-cfDNA to monitor for TCMR in pediatric kidney transplant recipients and performs better than creatinine.

Transplantation (including CMV, EBV & BK infections)

P1-153 - Longitudinal Kinetics of Plasma Donor-derived Cell-free DNA (dd-cfDNA) after Kidney Transplantation in Children

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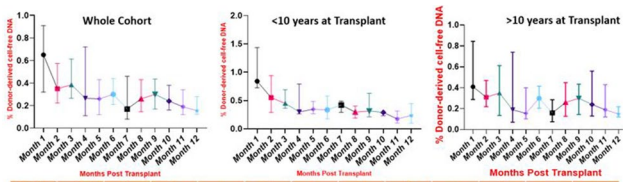
Purpose: In adult studies, the levels drop to a mean of 0.46% (± 0.21%) approximately 10 days after transplantation. (Gielis, 2018) Our aim was to determine if children would have similar kinetics, given the size mismatch between adult sized allografts and smaller sized recipients.
Methods: We accessed a biobank of 71 children with longitudinally collected and banked plasma samples monthly, drawn between 30 days and 12 months post-kidney transplant from 2013 onwards. We quantified dd-cfDNA in plasma by next generation sequencing using a targeted, multiplex PCR-based method for the analysis of single nucleotide polymorphisms (AlloSure, CareDx, Brisbane, CA). A subgroup of 237samples from 54 stable renal transplant recipients with no major infectious events, rejection events or delayed graft function were identified to study the dd-cfDNA kinetics over time.
Results: In this cohort, the median (25-75th percentile IQR) plasma % dd-cfDNA at 30 days post renal transplant was 0.65% (0.32 – 0.91 %), decreasing to 0.35% (0.22 - 0.57%) by month 2, to a median of 0.17 (0.08 - 0.46) % by month 6 and to a median of 0.16(0.12-1.28) % by month 12 post-transplant (Figure 2).When further stratifying into 2 groups based on the recipient age at transplant, in comparison to the >10 years group (171 samples), the <10-years recipient age group (66 samples) had a higher mean % dd-cfDNA through the entire first year post transplant. In the <10-year age group the median % dd-cf DNA did not reach <0.3 till 10 months post-transplant whereas in the >10 years age group the mean % dd-cfDNA reached < 0.3% by 4 months post-transplant.



Month Post transplant	1	2	3	4	5	6	7	8	9	10	11	12
Whole cohort												
25% Percentile	0.32	0.22	0.27	0.11	0.12	0.21	0.080	0.15	0.17	0.16	0.12	0.12
Median	0.65	0.35	0.39	0.27	0.26	0.30	0.17	0.26	0.30	0.24	0.19	0.16
75% Percentile	0.91	0.57	0.61	0.72	0.43	0.44	0.46	0.43	0.44	0.38	0.34	0.28
Less than 10 years at the time of transplant												
25% Percentile	0.73	0.29	0.37	0.27	0.27	0.18	0.29	0.19	0.21	0.23	0.10	0.10
Median	0.84	0.55	0.45	0.30	0.35	0.34	0.42	0.30	0.32	0.29	0.18	0.24
75% Percentile	1.4	0.94	0.69	0.79	0.48	0.58	0.49	0.40	0.63	0.29	0.32	0.45
Greater than 10 years at the time of transplant												
25% Percentile	0.29	0.22	0.14	0.070	0.10	0.21	0.075	0.13	0.15	0.13	0.12	0.12
Median	0.41	0.31	0.35	0.19	0.16	0.30	0.16	0.26	0.30	0.24	0.19	0.15
75% Percentile	0.85	0.47	0.61	0.74	0.40	0.42	0.29	0.45	0.44	0.56	0.43	0.22

Conclusions: % dd-cfDNA levels post-transplant are higher for a longer time in children versus adults. We attribute this difference to increased dd-cfDNA from the allograft and lower background self-cf-DNA from the lower body mass index of recipients.

Transplantation (including CMV, EBV & BK infections)

P1-154 - Prevalence of hypertension using ambulatory blood pressure monitoring in paediatric kidney transplant recipients treated with early steroid withdrawal immunosuppressive regimes.

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Objectives: To assess prevalence of hypertension and BP control following kidney transplantation (KT) using ambulatory blood pressure monitoring (ABPM) in children initiated on an early steroid withdrawal immunosuppression regimen.
Methods: Cross sectional study of children followed up in a single centre transplant clinic from April 2021 -March 2022 age >5 years who have been commenced on an early steroid withdrawal immunosuppression regimen.
Results: A total of 50 patients completed a successful 24-hour ABPM monitoring. The mean age was 13.7 years (range 8-18) and 65% of patients were male. The average time since kidney transplantation was 3.6 years and the mean estimated glomerular filtration rate (eGFR) was 61ml/min/1.73m2 (range 32-96). Using body mass index standard deviation scores 12% were overweight and 6% were obese. A total of 24% of patients were on an antihypertensive medication at the time of their study. A mean arterial pressure less than the 50th centile was recorded in 62% of the cohort over the 24-hour period. Average systolic blood pressure (BP) recordings were below the 50th centile for 82% of patients and no patients had an average systolic BP above the 90th centile. The average diastolic BP was less than 50th centile in 53% patients with 30% and 9% having an average diastolic BP in the 50-90th and above the 90th centile respectively. A nocturnal BP dip of greater than 10% was observed in 59% of patients.
Conclusions: There appears to be a low prevalence of hypertension as determined by ABPM in children initiated on early steroid withdrawal immunosuppression. BP control in this population appears to be excellent with majority having MAP and systolic values <50th centile.

Transplantation (including CMV, EBV & BK infections)

P1-155 - Longitudinal monitoring of Torque-Teno virus loads after kidney transplantation may predict opportunistic viral infections in pediatric transplant recipients

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Background: Careful balance of immunosuppression is essential to minimize the risk for infectious disease and rejection by alloimmunity, the major cause of late graft failure in kidney transplantation (KTX). Torque-Teno virus (TTV) plasma load was identified as a marker of immune status after solid-organ transplantation, correlating with immunosuppressant dosage in pediatric KTX patients. Our aim was to investigate TTV load association with and prediction of the major opportunistic viral infections, e.g., Epstein-Barr virus (EBV), cytomegaly virus (CMV), BK polyomavirus (BKV), and JC polyomavirus (JCV) in pediatric KTX during follow-up.
Methods: All pediatric patients at the Medical University of Vienna with a post KTX time of >3 months were included. All viral loads were routinely measured every four to eight weeks by quantitative PCR. Associations and predictions of log10 TTV loads with log10 EBV, CMV, BKV, and JCV loads as well as for relevant cut-off values were computed with generalized poisson mixed models with random slopes and intercepts for each patient over time accounting for temporal autocorrelation and mixed effects logistic regression, respectively.
Results: 72 pediatric KTX recipients were included. Baseline characteristics and primary kidney disorders are displayed in Table 1. TTV loads were significantly associated with CMV loads (p=0.008, p=0.0005), BKV plasma loads (p=0.02, p=0.03), BKV urine loads (p=0.01, p=0.005), and JCV loads (p=0. 000002, p=0.02) on the same and for the next visit, respectively. TTV loads were able to significantly predict infection above literature-based cut-off levels for CMV (p=0.0000001, p=0.000009), BKV plasma loads (p=0.002, p=n.s.), and BKV urine loads (p=0.04, p=0.00001) for the same and next visit, respectively. Associations with EBV were not significant.
Conclusions: This study is the first to significantly associate TTV loads with the occurrence of clinically relevant viral infections (CMV, BKV, and JCV), numerically and above relevant cut-offs on the same or the next visit, in pediatric KTX.

Table 1. Baseline characteristics and primary kidney disorders.

Primary kidney disorders	N	%
CAKUT	35	49
Glomerular disorders	15	21
Polycystic kidney disease	9	13
Congenital nephrotic syndrome	9	13
Metabolic disorders	2	3
Other	2	3
Baseline KTX characteristics	**N**	**%**
Male	47	65
Living Donors	45	63
Basiliximab induction	72	100
Tacrolimus	64	89
Cyclosporin A	4	6
Sirolimus	3	4
w/o calcineurin- or mTOR-inhibitor	1	1
Mycophenolate mofetil	61	85
Azathioprine	5	7
w/o antiproliferative substance	6	8
Steroids	71	99
	Median	**IQR**
Age (years)	12.2	8.0-15.8
Age at KTX (years)	8.1	3.4-13.0
Time post KTX (months)	19	3.3-63
HLA mismatch (n)	3	2-3
Creatinine (mg/dl)	0.89	0.54-1.31
eGFR (ml/min/1.73m²)	96.1	75.9-134.3
Study period (years)	3.5	0.7-6.1
Follow-up time (years)	6.6	0.9-19

CAKUT = congenital anomalies of the kidney and urinary tract, eGFR = estimated glomerular filtration rate

Transplantation (including CMV, EBV & BK infections)

P1-156 - Long term outcomes of paediatric kidney transplant in New Zealand

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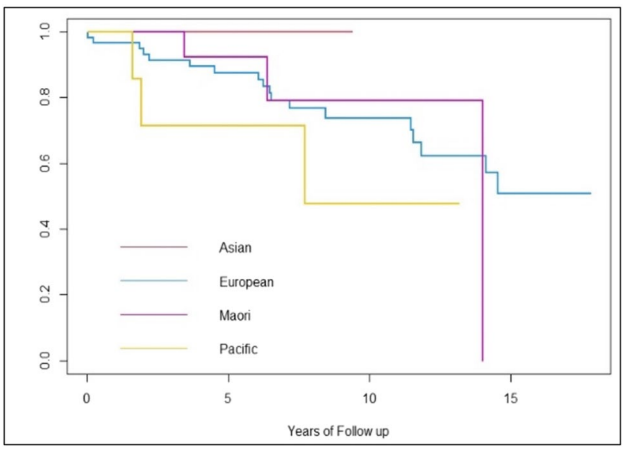
Background: Paediatric kidney transplantation (PKT) in New Zealand is provided at Starship Children's Hospital. Long term outcomes are reported in combination with Australian sites via Australia and New Zealand Dialysis and Transplant Registry (ANZDATA). However, detailed analysis of long-term outcomes for children in New Zealand is limited.
Aims: Our primary aim was to determine PKT graft survival in New Zealand children, including for Māori and Pasifika ethnicities. Our secondary aims were to i) determine longitudinal PKT graft function, ii) determine predictive factors for PKT graft dysfunction and graft loss.
Methods: A retrospective cohort study of children (<18 years) who received a PKT at Starship Hospital from 1 January 2002 to 31 December 2018 with minimum one year follow-up post-transplant was performed. Donor data was obtained from ANZDATA. PKT graft survival was analysed via Kaplan-Meier method. Cox Regression analysis examined the relationship between PKT survival and covariates of interest.
Results: Eighty-eight patients were included. PKT graft survival was 88%, 74% and 48% at five, ten and fifteen years post-transplant respectively. Pasifika children had a 48% PKT graft survival at ten years and Māori children had no functioning PKTs at fifteen years (Figure 1). There were no functioning deceased donor PKTs at fifteen years. Viral load presence, proteinuria at one year, and non-Asian ethnicity were predictors of reduced graft survival. The mean estimated glomerular filtration rate was 56 mL/min/1.73m^2, 46 mL/min/1.73m^2 and 46 mL/min/1.73m^2 at five, ten and fifteen years post-transplant respectively. The number of rejection episodes and deceased donor source was associated with reduced graft function at ten years post-transplant.

Figure 1: Kidney graft survival by ethnicity



Conclusions: Our overall PKT graft survival rates post-transplant are comparable (if not better) to other paediatric centres internationally. However, our Māori and Pasifika children have worse outcomes. Equity focused interventions are needed to promote improved outcomes for Māori and Pasifika children and youth.

Transplantation (including CMV, EBV & BK infections)

P1-157 - Delayed graft function: a single center experience

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Introduction: Delayed graft function(DGF)is defined as the need for dialysis in the first transplantation week.
Objectives: 1)to analyze our prevalence of DGF; 2)to evaluate risk factors and related conditions, and 3)to determine long-term outcome.
Methods: we evaluated patients with cadaveric grafts assisted between 1/2002-12/2021. We determined those with DGF(G1) and without DGF(G2). We evaluated donor and recipient age, vascular anastomosis(VAT) and cold ischemia time(CIT), HLA matching, complications in the operating room(COR), renal biopsies(RB), rejection episodes(Rx) during the first year and graft function at last follow-up. Statistic analysis:chi-square.
Results: we evaluated 100 patients.36 patients developed DGF(36%).Recipient age was 14.9 months in G1, and 143.8 months in G2.Donor age was 26.5 years in G1 and 21.3 years in G2. 7/35 donors in G1 were >40y vs 6/61 in the G2(p: 0.15). CIT was 20.4 h in G1 and 19.6 h in G2. CIT > 24 h was found in 10/36(27.7 %) in G1 vs. 10/64(15.6 %) in G2(p: 0.14).VAT was 59.8 min in G1 vs. 55.8 min in G2. 21/36 patients in G1 had 2 HLA matches(58.3 %) and 15 had 3 or more(41.7 %), vs 34/64(53.1%) and 30/64(46.9%) in G2, respectively. COR were seen in 16 patients in G1(45.7 %) and 35(45.4 %) in G2, mostly hypotension.RB were performed in 16/36(44.4%) patients in G, and 14(87.5 %) had findings of acute tubular necrosis(only 2 RB in G2).Rx during the first year were diagnosed in 16/36(44,4%) patients in G1 and 15/64(23.4 %) patients in G2(p<0.03).At last follow-up, nonfunctioning kidneys were found in 4/36(11,1%) in G1 and 7/63(11,1 %) in G2.
Conclusions**:** 1)DGF prevalence was 36 %;2)We didn¨t observe relationship with donor and recipient age, VAT and CIT, HLA matching, and COR; donor age >40y shows some tendence; ATN was the most frequent finding in RB and there were more Rx in G1;3)At follow-up, nonfunctioning kidneys were similar in both groups.

Transplantation (including CMV, EBV & BK infections)

P1-158 - The mode of kidney replacement therapy (KRT) influences the carotid intima-media thickness in children and adolescence

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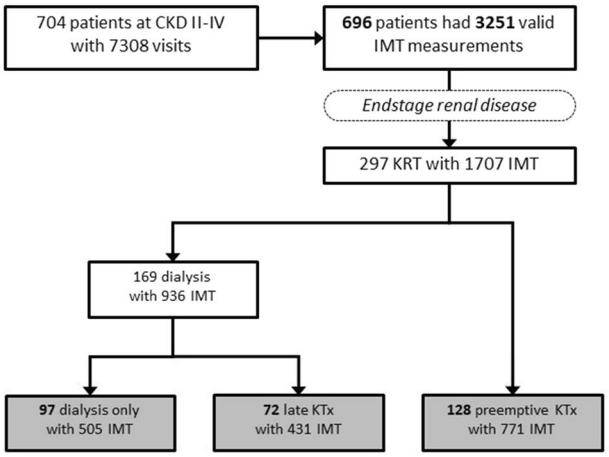
Long-term survival of children with chronic kidney disease (CKD) and kidney transplantation (KTx) is determined by cardiovascular (CV) morbidity. Carotid intima media thickness (IMT) is a measure of atherosclerosis and an important predictor for CV endpoints such as myocardial infarction and stroke in adults. Our aim was to elucidate how different KRT modes affect IMT in children with CKD and KTx.

This investigation is based on data from the international multicenter prospective 4C (Cardiovascular Comorbidity in Children with CKD) study, which investigated 704 children annually over a period of 10 years. The primary endpoint of our analysis was IMT. We differentiated between patients receiving preemptive KTx, late KTx (with previous time on dialysis) and dialysis. Multivariable linear mixed models were employed. In the course of the 4C study, almost half of the patients required KRT (N=297, Fig. 1A). Mean follow up time was 63±27 months, mean age at KRT start was 14.3±3.1 years and 36% were girls. Mean time on dialysis was 18±14 months for the late KTx and 28±26 months for dialysis group. A mixed model was constructed with IMT as the dependent variable (Fig. 1B). Higher IMT values were associated with longer time in the study and the last IMT measurement prior to KRT start. To study the effect of different KRT modes, we introduced an interaction term including KRT mode and time on KRT. We demonstrate that only preemptive KTx significantly reduced IMT progression (p=0.0081), while late KTx and dialysis did not. Further analyses will focus on underlying factors for this difference. Our data suggests that preemptive KTx slows down the atherosclerotic process. A better understanding of the potential long-term benefits of preemptive KTx should help to introduce preventive measures early on.

A



B

Model for IMT*, mm				
Effect		**β**	**SE**	**p**
Intercept		0.2119	0.0197	**<.0001**
Age, years		0.0009	0.0007	0.1833
Sex	(ref. male)	-0.0008	0.0033	0.815
Height, m		0.0082	0.0129	0.5265
Time, years		0.0057	0.0011	**<.0001**
Last IMT before KRT start, mm		0.5070	0.0289	**<.0001**
Time after preemptive KTx, years	(ref. CKD)	-0.0048	0.0018	**0.0081**
Time after late KTx, years	(ref. CKD)	-0.0037	0.0024	0.1298
Time during dialysis, years	(ref. CKD)	-0.0024	0.0017	0.1679

Abbreviations: CKD, chronic kidney disease; IMT, Intima-media thickness; KTx, kidney transplantation; mm, millimeter; β, regression coefficient; SE, standard error; m, meter.
*__Explanatory note__: center, individual patients and time are accounted for as random effects

Transplantation (including CMV, EBV & BK infections)

P1-159 - Humoral and cellular response to COVID-19 mRNA vaccination in Children with end-stage kidney (ESKD) disease.

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Effective mRNA vaccines against SARS-CoV-2 became widespread available during the past year allowing for the unique opportunity to study immune responses to this novel vaccine-type in various naïve populations, both in health and disease. While adult patients with ESKD demonstrated a poor immune response, especially after kidney transplantation (KTx), data for the pediatric population is very limited. We initiated a longitudinal observational study on humoral and cellular response in children under the age of 16 with ESKD (KTx/dialysis). We measured anti-spike antibodies (commercial kit) and SARS-CoV-2-specific T cells reactive against spike proteins of several variants (ELISPOT assay).
From this still ongoing study, we analyzed 19 children (18 KTx, 1 dialysis) 5-14 weeks after their second dose of BNT162b2/Tozinameran. Median age of the participants was 14.9 years (IQR 1.5), median eGFR was 56 mL/min/1.73 m2 (IQR 45) and median time after KTx was 6.2 years (IQR 5.7). Immunosuppression included CNI with mTOR inhibition (n=14) or MMF (n=4), 9 patients received steroids. Antibodies were detected in 68%, only 4 patients displayed a strong response (>15,000 U/ml, all KTx, Fig.1A). In contrast, SARS-CoV-2-specific T cells were detected in more than 90% (Fig.1B). High and intermediate T cell responses were between 59% and 76% depending on the SARS-CoV-2 variant. Among the 6 patients without detectable antibodies 2 displayed a low and 2 an intermediate T cell response.
In summary, strong immune responses were rare (21% humoral, 18-24% cellular) in our cohort of mainly KTx recipients. More than a quarter did not develop any antibody response, but only about 10% did not show a virus-specific T cells. Yet, most of those humoral non-responders had a detectable cellular response. The durability and protection of the observed immune responses will be further followed. We will expand the cohort by inclusion of patients <12 years.

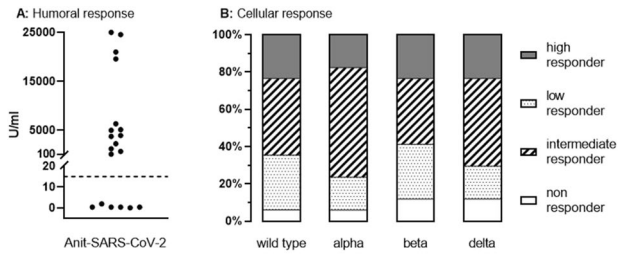

Figure 1: Immune response of 19 children after kidney transplantation or under dialysis 5-14 weeks after their second vaccination with BNT162b2/Tozinameran.
A: Antibody levels against SARS-CoV-2 spike protein receptor binding domain. Threshold 15 U/ml (dashed line).
B: SARS-CoV-2-specific T cells against different virus variants.

Transplantation (including CMV, EBV & BK infections)

P1-160 - COVID 19 pandemic resulted in significant weight gain in in teenagers after kidney transplantation

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Objectives: The COVID-19 pandemic has led to widespread change of lifestyle, restrictions of social relations and activities. The required lockdowns caused modifications in eating habits, physical activities and psychological distress. This not only has consequences for adults, but also for children and adolescents. The COVID-19 pandemic has been linked to significant weight gain in the general population, but its impact on children and adolescents after kidney transplantation (KTx) is unknown.
Methods: We retrospectively evaluated body mass index SD scores (BMI-SDS) between September 2019 and September 2021 in 132 pediatric KTx patients followed up at three German pediatric nephrology centers. The patients were categorized according to age (0-11.9 years vs 12-18 years) and sex (female vs. male) in four groups. Data were assessed by a linear mixed model approach.
Results: There was no significant change in BMI-SDS in children (0-11.9 years), irrespectively of sex (boys -0.11 SDS, p=0.22; 0.05, p=0.49). By contrast, a significant increase in BMI-SDS was noted in both male (0.24 SDS) and female (0.20 SDS) teenagers (each $p<0.05$). In addition, the proportion of obese teenagers tended to increase from 12% to 19% (p=0.08). Conclusion
The COVID19 pandemic was associated with a significant increase in standardized BMI values in adolescents but not in children after KTx. This may further increase the cardiovascular risk in the former population.

Transplantation (including CMV, EBV & BK infections)

P1-161 - Immunosuppression and recurrence free parental donor kidney transplant in patient with previous graft loss secondary to recurrent FSGS using prospective a/b T cell, CD19 depleted haploidentical parental stem cell transplant

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This 20-year old male with FSGS since age 3, progressed to ESKD and received a maternal donor kidney transplant at age 9. Recurrent FSGS caused graft loss in 3 months despite steroids, cyclophosphamide, IV cyclosporine, rituximab, and plasmapheresis. He remained on dialysis for a decade.

After informed consent, he received an α/β T cell depleted, CD19 depleted stem cell transplant. Conditioning was with 7.5 mg/kg rabbit anti-thymocyte globulin, 100 mg/kg cyclophosphamide, fludarabine (27.5mg initial dose & pharmacokinetics determined subsequent 3 doses) melphalan 100 mg/m², rituximab 200 mg/m² and a single dose of 200 cGy total body irradiation. Stem cells mobilized with plerixafor were harvested from the 5/10 HLA matched father, then αβT and CD19B depleted in a GMP facility. He received 13.6×10^6/kg CD34 positive stem cells and 0.1×10^5/kg TCR α/β T cells after depletion. Platelets and neutrophils engrafted day 14, with his course complicated by acute Graft vs Host Disease (Skin Grade 4, Liver Grade 2) which responded to therapy, and a readmission for intensive nutrition, multidisciplinary symptom management and rehabilitation.
On SCT day #362 he received a living donor kidney transplant from the SCT donor with no induction immunosuppression. Post-transplant immunosuppression was oral prednisone starting at 0.5mg/kg/day and tapered off by Post Kidney Transplant day #30. He was maintained on tacrolimus with a target level of 7ng/ml (originally for GVHD prophylaxis). At latest follow-up Post Kidney Transplant Day #60, his estimated CKiD U25 GFR is 66ml/min/1.73M^2 and urine protein/creatinine ratio is normal at 0.2mg/mg. Tacrolimus will be discontinued in another month. The post-transplant course was uneventful.
After 10 years of dialysis, this patient received a stem cell transplant followed by a kidney transplant from the same donor. There is no evidence of FSGS recurrence 2 months post-transplant, no GVHD and in another month the patient will be free of immunosuppressive medication.

Transplantation (including CMV, EBV & BK infections)

P1-162 - Nephropathy due to BK virus infection in pediatric renal transplant patients

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Nephropathy due to BK virus infection in pediatric renal transplant patients.

Introduction: Primary infection by human BK polyomavirus (BKV) occurs in childhood, it is endemic, in healthy children they will remain asymptomatic. When cellular immunity is altered, the virus can be reactivated, for this reason it is particularly important to study it in the kidney transplant population.
Clinical Summary: adolescent, male, 15 years old, history of chronic kidney disease secondary to uropathy. Hemodialysis for 2 years. Kidney transplant in 2018 related living donor. Donor and recipient positive for Epstein-Barr Virus (EBV), Toxoplasma and Cytomegalovirus (CMV), the latter was treated with Ganciclovir followed by Valganciclovir per protocol. Initial immunosuppression Tacrolimus, Mycophenolate Mofetil, Basiliximab and Methylprednisolone, maintenance Prednisone, Tacrolimus and Mycophenolate. Post-transplant discharge 10 days, creatinine: 0.63 mg/dl. Two months post-transplantation, the first increase in creatinine was presented, laboratory investigation and negative images, maintaining altered creatinine values, without other altered symptoms, with improvement by increasing the water intake. Four months post-transplantation, BVK in blood viral load, by

decreasing immunosuppression, creatinine improved and BVK was not detectable. At 10 months post-transplant, new creatinine alteration with detectable increasing BVK load, Sirolimus was started, continued with low-dose Tacrolimus, without Mycophenolate. Renal biopsy ruled out acute and humoral cellular rejection. Given progressive and sustained creatinine and BVK load, he received gamma globulin for 6 months. At the end of this scheme, it turned out that the viral load, creatinine was stationary between 1.8mg/dl.
Conclusion: The importance of making the differential diagnosis between acute rejection and BK infection lies in the fact that the conduct regarding immunosuppressive therapy is opposite. Periodic laboratory monitoring is essential for early diagnosis and timely treatment to stop kidney damage. When it is installed, it does not regress with any treatment and conditions graft survival.

Transplantation (including CMV, EBV & BK infections)

P1-163 - Sixteen kidney transplantations in childhood cancer survivors

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Background: As the life prognosis of pediatric patients with malignancies improves, late-developing kidney dysfunction becomes a problem. To evaluate the pros and cons of kidney transplantation in childhood cancer survivors (CCS), the post-transplantation course and life prognosis of CCS at our hospital were evaluated.
Methods: Of the 521 pediatric patients who received a kidney transplant at our hospital between January 1975 and December 2020, those with CCS at the time of transplantation were analyzed.
Results: Sixteen of the 521 patients were CCS and had a median age at cancer diagnosis of 1.3 years (range: 0.5-11.0 years). The malignancies included Wilms tumor (n=11), neuroblastoma (n=4), and hepatoblastoma (n=2).
The causes of kidney failure were Denys-Drash syndrome-associated nephropathy (n=7), treatment-related nephropathy (n=7), CAKUT (n=1), and unknown (n=1). Kidney transplantation was performed at the median age of 7.2 years (range: 4.2-20.7 years) and the median interval of 5.0 years (range: 2.4-17.7) after completion of cancer treatment.
During the median observation period of 4.6 years (range: 0.0-21.3 years) after kidney transplantation, two patients experienced kidney failure and required replacement therapy (0.2 years and 21.3 years post-transplantation, respectively), one patient died from ARDS immediately after surgery, and one patient with a previous Wilms tumor had two tumor recurrences in the lung at 4.9 years and 7.2 years, respectively, after transplantation, but is still alive.
Discussion: In kidney transplantation in CSS, multiple organ damage caused by the drugs used to treat the cancer and the recurrence of post-transplantation malignancies can be a problem. In the present study, one patient experienced repeated tumor recurrences, but no other specific adverse events were noted, suggesting that kidney transplantation can be performed safely in CCS.
Conclusion: Kidney transplantation may be a viable option for kidney replacement therapy in CCS.

Transplantation (including CMV, EBV & BK infections)

P1-164 - Post-transplant diabetes mellitus in Epstein syndrome

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Background: Epstein syndrome (ES) caused by *MYH9* gene abnormality is a disease associated with giant platelet thrombocytopenia and progressive nephritis, leading to CKD stage 5 in severe cases. Recently, the involvement of single nucleotide polymorphisms in the *MYH9* gene in the development of type 2 diabetes mellitus has been reported.
Methods: We retrospectively investigated post-transplant glucose intolerance in 4 male ES patients (case A, B, C, and D) who had undergone living donor kidney transplantation at our department for more than 4 years.
Results: The age at transplantation of cases A, B, C, and D was 35, 15, 17, and 19 years, respectively. The genotypes were *p.S96L* in 1 case and *p.R702C* in 3 cases, both of which were the most severe mutations in ES. HbA1c at the time of pre-transplant examination was in the normal range in all cases, and oral glucose tolerance tests at the time of pre-transplant examination was borderline in case A, but normal in the others. All patients were managed with maintenance immunosuppressive drugs, mainly methylprednisolone, tacrolimus, and mycophenolate mofetil, and their transplant kidney function remained relatively good. Cases A, B, and C were diagnosed with post-transplant diabetes mellitus (PTDM) within 2 years of transplantation, and were treated by reduction of methylprednisolone and tacrolimus and administration of DPP-4 inhibitors. In cases A and B, a rapid worsening of HbA1c was observed more than 6 years after transplantation, requiring the introduction of insulin self-administration.
Conclusion: PTDM was observed in 75% of our ES recipients. Their high prevalence of PTDM and younger age of onset of PTDM compared to general kidney transplant recipient population suggested that *MYH9* gene abnormalities may have been involved in the worsening of post-transplant glucose intolerance. In ES recipients, it was considered necessary to pay attention to the onset of PTDM.

Transplantation (including CMV, EBV & BK infections)

P1-165 - A case of enteritis caused by Yersinia enterocolitica after kidney transplantation

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In pediatric post-kidney transplant cases, the diagnosis of gastrointestinal symptoms is often difficult because of the wide variety of causes, including infections, drugs, and post-transplant lymphoproliferative disorder (PTLD). Yersinia enterocolitica (Y. ent) infection is a relatively common infection, but it is often overlooked because of the special conditions required for its culture. We report a case with Y. ent infection that was difficult to diagnose. A 14-year-old boy with end-stage kidney failure due to focal segmental glomerulosclerosis underwent living donor kidney transplantation at the age of 12. One year and 5 months after transplantation, he was diagnosed

with active antibody-mediated rejection, and immunosuppressive drugs were increased. 2 weeks later, fever, diarrhea, and abdominal pain appeared and persisted, and he was hospitalized. After admission, the immunosuppressive drugs were reduced, but the diarrhea continued. Abdominal ultrasonography (US) showed thickening of the terminal wall of the ileum, and colonoscopy revealed a map ulcer at the terminal ileum and aphthae throughout the colon. We initially considered the possibility of CMV enteritis and started ganciclovir, but fever and diarrhea persisted. Since the serum CMV antigenaemia was negative and the tissue CMV-IHC was negative, CMV enteritis was considered negative. Next, we suspected PTLD due to EBV enteritis because the pathology of lymphofollicular hyperplasia forming erosive ulcers, but since serum EBV-PCR was negative and tissue EBER-ISH was negative, EBV enteritis was considered unlikely. We suspected Y. ent infection based on the thickening of terminal wall of the ileum and lymphadenopathy caused by US, and performed stool culture. Y.ent was detected in special stool culture on cefsulodin-Irgasan-novobiocin (CIN) agar medium. Fever and diarrhea improved with antibiotic therapy, and US findings improved. Y.ent infection should not be overlooked when diagnosing gastrointestinal symptoms in post kidney transplant patients. Diagnosis of Y.ent infection requires CIN agar medium required for its culture.

Transplantation (including CMV, EBV & BK infections)

P1-166 - Mycophenolate-induced gastrointestinal complications in children post kidney transplant

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Background: Kidney transplantation is the optimal therapy for children with end stage kidney disease (ESKD) and outcomes have improved with newer immunosuppressive strategies. Gastrointestinal (GI) complications remain common post kidney transplant and are a cause of significant morbidity and even mortality, with diarrhea being the most common symptom. Causes include infections, immunosuppressive drugs, post-transplant lymphoproliferative disease, post-transplant inflammatory bowel disease, and rarely graft versus host disease. Mycophenolate mofetil (MMF) is a commonly used immunosuppressive medication in organ transplantation and is known to cause nausea, vomiting, dyspepsia, reflux, diarrhea, and MMF-induced histologic changes including esophagitis, gastritis, enteritis and colitis. In pediatrics, severe GI s complications related to MMF have rarely been described in the literature.
Methods: We report three cases of severe GI disease in pediatric kidney transplant recipients attributed to MMF leading to hospitalization : i) a 15 year old male with severe oral ulcerations, odynophagia, diarrhea and weight loss, ii) a 13 year old female with severe acute on chronic diarrhea and ii) a 13 year old male with poor appetite, chronic diarrhea and abdominal pain, poor weight gain and stunting. MMF was tolerated for months to years prior to the onset of GI symptoms.
Results: In all patients, alternative causes were ruled out and gastroscopy and colonoscopy were consistent with MMF-induced enteritis. Their symptoms rapidly improved with sustained resolution after the discontinuation of MMF, further reinforcing the causal association.
Conclusions: MMF can cause severe GI disease in pediatric kidney transplant recipients with varied presentations. These cases highlight the importance of considering MMF-induced GI disease in children with kidney transplant and GI symptoms, regardless of the timing of GI symptom onset from MMF initiation. There was prompt resolution with discontinuation of the drug. These cases add to the limited literature regarding treatment of MMF-induced GI disease post kidney transplant.

Transplantation (including CMV, EBV & BK infections)

P1-167 - Validation of a prediction system for risk of allograft loss (iBOX) in pediatric kidney transplant recipients

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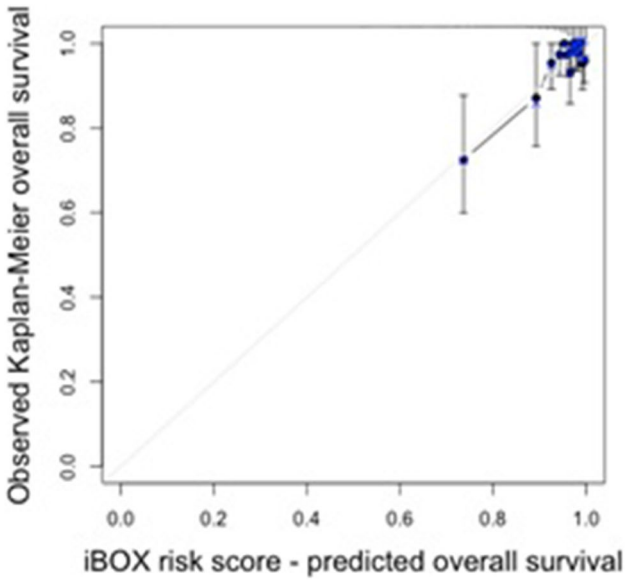
Background: Kidney allograft loss is a common cause of end-stage renal disease but accurate prediction models of kidney allograft loss are lacking in children. The iBOX system has been broadly validated among adults. We aimed to validate the iBOX system in a large international cohort of pediatric kTx recipients.
Methods: In this observational study, we used data from pediatric (<21) patients transplanted between 2005 and 2017 from 20 institutions in Europe and the United States. Patients with functional parameters (eGFR and UPCR), donor specific antibody and biopsy results (Banff scores g, ptc, cg, i, t, IFTA) were included. Individual predictions of allograft loss were obtained by applying the iBOX score on our data. The prediction performances of the model in our population were assessed via discrimination (c-statistics) and calibration.
Results: 573 kTx recipients were included. Median time from transplantation to evaluation was 1.0 [0.5-2.0] year with a mean age at evaluation at 12.1(5.5) years and mean follow-up after transplantation 5.1 (2.8) years. 5-year death-censored graft survival from evaluation was 95%. At the time of evaluation, mean eGFR and uPCR were 65.5(29.6)mL/min/1.73m2 and 0.25(1.2)g/g, respectively. 118 (20.6%) of the patients had DSA. The iBOX system showed good discrimination with a c-statistic of 0.81 and good calibration (Figure 1).
Conclusion: The iBOX system demonstrated high accuracy in predicting kidney allograft loss in children with performances similar to those reported in adults.

Figure 1: Calibration between the predicted risk and the observed number of allografts lost at 5 years.



Transplantation (including CMV, EBV & BK infections)

P1-168 - Effect of Angiotensin II Type 1 Receptor (AT1R) Antibodies on graft function and survival in paediatric kidney transplant recipients

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Introduction: Human leukocyte antigen (HLA) donor specific antibodies (DSA) are implicated in antibody-mediated rejection (AMR), graft dysfunction and failure in kidney transplant (KT). Evidence suggests that non-HLA antibodies including AT1R also play a role in AMR, impact graft function and survival. Data is variable and limited in paediatric KT cohorts.
Aim: To assess the effect of AT1R antibodies on rejection, graft function and survival in paediatric KT recipients.
Method: A retrospective cohort study was conducted across two paediatric KT centers. Recipients between 2007-2021 with at least one AT1R antibody level (pre and/or post KT) were eligible. Demographic data, graft function, episodes of biopsy proven rejection, development of de novo DSA, proteinuria and hypertension were collated.
Results: Of 83 eligible individuals, 60% recorded a positive AT1R antibody level (>17 U/ml), 21% were at risk (10-17 U/ml) and 19% negative (<10 U/ml). Age at and source of KT, cause of end stage kidney disease, maintenance immunosuppression, HLA matching, EBV and CMV status did not differ with level of AT1R antibody. Graft function at 1, 3 and 5 years post KT, de novo DSA development, hypertension, proteinuria and rejection episodes (AMR, T-cell mediated or mixed) were not statistically different between groups. In total three individuals had graft failure, one negative for AT1R antibodies and two positive (p-value 0.60).
Conclusion: This is the largest study assessing effect of AT1R antibodies in paediatric KT recipients. We found no correlation between AT1R antibodies and rejection, graft dysfunction or failure. Whilst paediatric KT recipients have a high prevalence of AT1R antibodies, we did not detect clinical significance in outcomes.

Transplantation (including CMV, EBV & BK infections)

P1-169 - Assessment of HLA incompatibility at the molecular compared to antigenic HLA level enables better prediction of graft function deterioration in paediatric kidney transplantation.

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Introduction: HLA mismatching has a detrimental effect on graft survival after paediatric kidney transplantation. Assessment of HLA incompatibility at the molecular level (molecular HLA mismatch; molMM) has emerged as a promising method for predicting primary alloimmunity risk. In this study, we aimed to assess whether molMM compared to conventional antigenic mismatching (antMM) enables better prediction of kidney allograft function deterioration.
Methods: We performed a retrospective analysis of 177 paediatric patients from the ABMR study of the CERTAIN registry. Only five patients experienced graft loss. Therefore, we used the time to 50% reduction in eGFR, from month-3 post-transplant baseline, as a surrogate endpoint for long-term graft loss (eGFR-50). HLA molMM was assessed using the Cambridge amino acid mismatch score (AAMS). Survival analysis was performed using Cox models, adjusted for donor and recipient baseline characteristics.
Results: 27 (15%) patients met the primary outcome. In multivariable analysis, recipient and donor age, baseline eGFR, and re-transplant status had a significant association with eGFR-50. Importantly, only mismatches at HLA-DQα1β1, and not at other loci, were associated with the primary outcome (adjusted HR (aHR) 10.2; 95% CI, 10.1-10.4 per 10 AAMS increase). There was a wide range of AAMS values (0-49) within each HLA-DQ antMM (0-2). We used a predetermined molMM threshold (AAMS=16 derived from analyses of donor-specific antibody) to classify patients into "low" and "high" risk. Patients clustered according to their molecular risk ("high" v "low"), regardless of their antMM. Additionally, patients with "low" risk for both alleles ("low/low") had the best outcomes ("low/high": aHR 4.7, 1.9-11.4, p<0.05; "high/high" aHR 5.7, 1.4-22.7, p<0.05 versus "low/low", Figure 1).
Conclusion: Compared to antMM, molMM showed better stratification of outcomes whilst increasing the number of patients in the low risk group ("low/low" n=100, v 0 antMM n=65). Further validation of molMM in independent cohorts is required before clinical implementation.

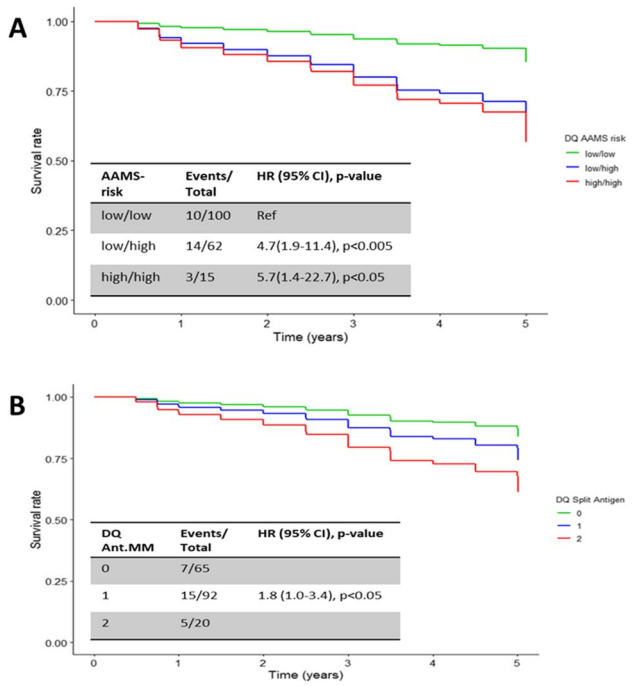

Figure1: Survival analysis for GFR50 outcome based on molMM (A) and antMM (B). Survival curves were adjusted for baseline eGFR, recipient age, donor age and transplant number. Hazard ratios were calculated using multi-variable Cox analysis.

Transplantation (including CMV, EBV & BK infections)

P1-170 - A Longitudinal Study Of Long-Term Renal Outcome After Pediatric Liver Transplantation In Relation To CNI Exposure.

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Introduction: CKD after liver transplantation (LT) is a reported in 20-30% of children. The underlying cause is multifactorial, however CNI-based immunosuppression is almost universal and renal histological changes related to CNIs were demonstrated in 48% of liver recipients with renal failure. Variation in CNI exposure are believed to be important in for developing CNI nephrotoxicity.
Aim: describe the long-term renal outcome of pediatric LT recipients in relation to tacrolimus disposition and pharmacogenetic background.
Methods: Single center retrospective study with a standardized annual follow-up of renal function (eGFR, mGFR: 51Cr-EDTA clearance, proteinuria) and elaborate pharmacokinetic assessment (C0, AUC0-12h) in recipients of a liver allograft (≤19 years), between 1998-2019. Relevant genetic variants for tacrolimus (*CYP3A5* and *ABCB1*) were determined in recipients and donors. Evolution of renal function and tacrolimus exposure was evaluated using linear mixed models.
Results: We included 26 children with 244 visits (age transplantation: 5.5yrs; follow-up: 10.4yrs). Mean eGFR was 109.3 (SE: 7.43) while mGFR was 91.34 ml/min/1.73 m2 (SE: 6.34), which were stable during follow-up. CKD≥2 was present in 32.8% of visits based on eGFR vs. 50% according to mGFR. CKD 3 was uncommon (4.1% and 6.2% resp.). Mean tacrolimus C0: 5.26 ng/ml (SE: 2.5), AUC0-12h : 72.7 ng*h/ml (SE: 30.3) and demonstrated a small decrease during follow-up. mGFR decreased by 1,95 ml/min/1.73m2 per 1 ng/ml increase of tacrolimus (SD 0,6; p: 0,02). No correlation between renal function and tacrolimus dose requirements nor pharmacogenetic background.
Conclusion: Renal function during follow-up after pediatric LT appears stable. However, mild CKD (based on mGFR) is common in children after LT, warranting follow-up into adulthood. Although absolute tacrolimus exposure has a mild depressing effect on GFR, we found no functional signs of progressive renal damage due to long-term CNI exposure under the current tacrolimus exposure

Transplantation (including CMV, EBV & BK infections)

P1-171 - Kidney transplantation in small children is associated with higher costs as compared to bigger recipients

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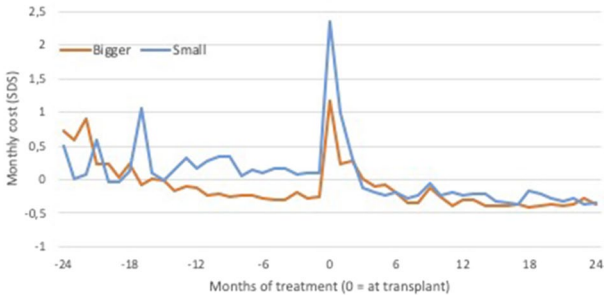
Objective: To explore the difference in the total standardized costs of kidney transplantation in small children (weight<15 Kg), when compared to bigger children.
Methods: Analysis of a database with 773,674 observations on costs information from 2009 to 2016. Each patient was observed for a different number of months, and the cost analysis involved 2 years before, at transplant, and 2 years thereafter. The analysis included costs with materials and medicines, orthoses, prostheses, and other special materials, hospital services (such as hemodialysis and apartment rates), diagnosis and therapy services. To model the costs, we employed the Nearest-Neighbor Matching approach, pairing each small child to a bigger patient who had the closest possible characteristics.
Results: We studied 256 children (155/256 small), with a mean age of 7 (SD=5) years, 64.5% male, and deceased donors in 84%. Mean follow-up was 25.6 (SD=20.2) months. In all analyses, the transplantation of a small child was associated with an increase in the total costs. Statistically significant effects (0.27 to 0.49 SDS) were found in the estimates of the total sample during the whole 4 years period and also at the transplantation phase. The weakest differences were found in the post-transplantation period. Counterintuitively, the pre-transplantation costs did not show statistically significant effects on econometric analysis. Perhaps the matching technique utilized, by comparing children with a similar follow-up before transplantation, purged the effect of the early start of transplant preparation in small children.
Conclusions: This study indicates that transplanting small children incur a higher average standardized accumulated cost, as compared to bigger recipients. The disparity occurs especially in the transplantation phase and the consumption of materials and equipment and hospital services (such as daily allowances) explain this difference. This information is innovative and can aid to prepare public policies in pediatric transplantation.

FIGURE 1 – Monthly costs (SDS) of treatment according to recipient weight.



Transplantation (including CMV, EBV & BK infections)

P1-172 - The lesser of 2 evils: bleed or clot? Utilizing an antithrombosis protocol after pediatric kidney transplantation

Marcos E Pozo[1], Aisha Ahmed[1], Aparna Hariprasad[1], Katherine Brandt[1], Caroline Lemoine[1], Riccardo Superina[1]
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Introduction: Antithrombosis protocols may prevent vascular complications but carry an increased potential for hemorrhagic complications. We present our experience with a protocol aimed at thrombosis prevention in selected kidney transplant patients (KT).
Methods: A retrospective review of our institutional KT database was performed (2015-2021). Patients with hypercoagulable states or a history of thrombosis received postoperative unfractionated heparin for clot prevention (AT group). The nAT group received no prophylaxis. Primary outcome was graft loss due to vascular thrombosis. Secondary outcomes included transfusion requirements, hematoma requiring intervention, and graft survival.
Results: One hundred and forty patients received 142 grafts. Seventy-five patients (52.8%) were in the AT group. Mean age at transplant was 12.2±5.2 and 9.9±6.0 years for nAT and AT groups, respectively (p=0.017). The most common diagnosis in the AT group was focal segmental glomerulosclerosis (18/75, 24%), and hypoplasia/dysplasia in nAT group (17/67, 25.4%). There was no difference between groups in proportion in pre-op dialysis, donor source, cold ischemia time, or operative time. The AT group had a higher proportion of intra-abdominal kidneys (32% vs. 14.9% p=0.029). Renal vein thrombosis occurred in 2/67 patients (3.0%) in the nAT group and none in the AT group. There were no arterial thromboses in either group. Blood transfusions were more common in the AT group (57.3% vs 38.8%, p <0.05) but the transfusion requirements were similar (19.4±18.9 versus 13.3±9.0 mL/Kg, AT vs nAT respectively). Two grafts were lost to thrombosis in the nAT patients but none in the AT group. The frequency of hematomas was higher in AT group (12.2 vs. 1.5%, p=0.033).
Conclusions: Our antithrombosis protocol proved safe, with a zero rate of graft thrombosis and acute graft loss in the population at risk, and a negligibly higher transfusion requirement. There was a higher rate of hematomas requiring interventions without affecting graft survival.

Table 1

Table 1. Outcomes with antithrombotic protocol for pediatric kidney transplants 2015-2021

Outcome(s)	nAT n=67	AT n=75	*p* value
Graft failure; n (%)	5 (7.5)	3 (4)	
Death with functioning graft	1	1	
Chronic rejection	1	2	
Graft thrombosis	2	-	0.597
Ureteral complication	-	-	
Recurrent disease	-	-	
Other	1	-	
Transfusion requirement; n (%)			
Yes	26 (38.8)	43 (57.3)	0.042
No	41 (61.2)	32 (42.7)	
Transfusion requirement (mL/Kg); mean (SD)	13.3 (9.0)	19.4 (18.9)	0.129
Hematoma; n (%)	1 (1.5)	9 (12.2)	***0.033***
Rejection episodes; n (%)	15 (22.4)	17 (22.7)	0.999
Graft survival	62 (92.5)	72 (96)	0.597

Abbreviations: nAT, no antithrombotic group (received no anticoagulation postoperatively); AT, antithrombotic group (received either prophylactic 10U/Kg unfractionated heparin or therapeutic 20U/Kg unfractionated heparin postoperatively)

Transplantation (including CMV, EBV & BK infections)

P1-173 - Successful pediatric kidney transplantation in a child with a thrombosed inferior vena cava avoiding total vascular exclusion of the liver

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Background: Long standing central venous catheters, chronic nephrotic syndrome or a hypercoagulable condition can lead to inferior vena cava (IVC) thrombosis complicating future kidney transplant (KTxp). Here we present the case of a successful KTxp performed in a child with a thrombosed IVC.
Case report: A 6-year-old female (weight 13.7 kg) with end-stage renal disease caused by congenital nephrotic syndrome Finnish-type also suffered from antithrombin III deficiency and had a history of multiple line-related thrombi. Preoperative imaging revealed a diminutive IVC and unsuitable iliac veins. The supra-hepatic IVC was patent. We planned to perform the venous anastomosis to the supra-hepatic IVC under total vascular exclusion of the liver.
A right kidney was allocated to our patient. A donor IVC extension was created using a TA stapler elongating the right renal vein. A trans-peritoneal approach was used for the transplant. The right liver was mobilized to the left exposing the IVC. The infra-hepatic IVC was completely replaced by a fibrous cord without a patent lumen (Figure 1A), but the retrohepatic IVC was found to be patent. It was encircled below the hepatic veins while controlling hepatic veins originating from the caudate lobe, avoiding total vascular exclusion of the liver. A donor iliac vein graft was first anastomosed to the retrohepatic IVC and the donor IVC extension graft to the donor iliac vein graft. The renal artery was anastomosed to the aorta (Figure 1B). After reperfusion, an intraoperative ultrasound confirmed vascular patency. The patient was discharged on therapeutic anticoagulation for 6 months. She is now 21 months after transplant with excellent graft function.
Conclusion: Pediatric KTxp can be complicated by congenital or acquired vascular anomalies. Infra-hepatic IVC thrombosis is not a contraindication to KTxp. A retrohepatic IVC anastomosis is a safe outflow alternative and avoids subjecting the liver to warm ischemia.

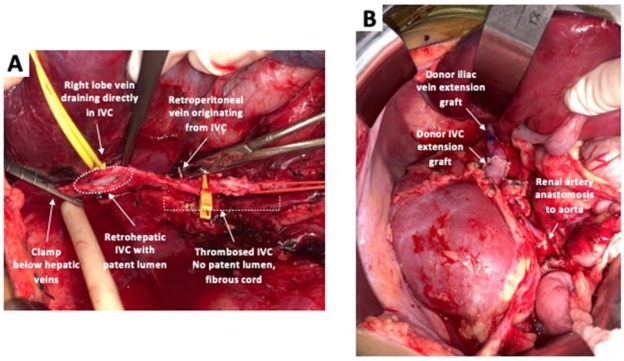

Figure 1. Intraoperative pictures: (A) Inferior vena cava (IVC) dissection revealed patency only at the retrohepatic portion which was chosen as the venous anastomotic site. (B) Renal graft after reperfusion showing patency of all vessels.

Transplantation (including CMV, EBV & BK infections)

P1-174 - Incident nephromegaly and kidney function in children with biliary atresia awaiting liver transplantation

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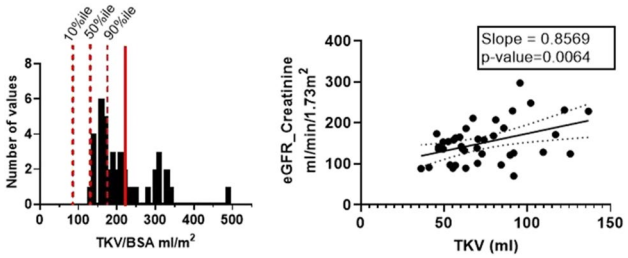
Background: The incidence of nephromegaly associated with biliary atresia (BA) and whether it contributes to improved or adverse renal outcomes is unknown. Hepatocyte growth factor (HGF) is overproduced during liver failure and is known to have kidney specific mitogenic, morphogenic, and anti-apoptotic properties.
Objective: To describe the incidence of nephromegaly in a large single center cohort of young BA patients awaiting liver transplantation and to evaluate the association between kidney size and renal function.
Methods: A retrospective cohort study of patients with BA listed for liver transplant from 2011 to 2020. Patients were excluded if they did not have a baseline ultrasound or CT scan and/or had any anomalies of the kidney and urinary tract. Data collection included demographic and clinical variables. Estimated glomerular filtration rate (eGFR) based on serum creatinine (Cr) was calculated using the modified Schwartz equation. The primary outcomes were total kidney volume (TKV) and TKV indexed to body surface area (BSA). Nephromegaly was defined as greater than the 90th percentile for TKV/BSA. Statistical analysis included descriptive statistics and linear regression analysis.
Results: A total of 41 patients met inclusion criteria. The mean age at the time of transplant was 0.99 years ± 0.54 years, 27/41 (66%) were female. The mean TKV/BSA was 217.82 ± 74.75ml/m^2 (Figure 1, left, solid red line) compared to a reference population where 171ml/m^2 = 90th percentile (dashed red line). Seventy-three percent (30/41) had a TKV/BSA ≥ 90th percentile. The eGFR_Cr significantly correlated with TKV (Figure 1, right).



Conclusion: The incidence of nephromegaly in a large cohort of children with BA awaiting liver transplantation is significant. A higher TKV correlated with a higher eGFR_Cr suggesting hyperfiltration and/or resilience to renal injury during periods of stress. Future studies should investigate the role of HGF and nephromegaly on long term outcomes.

Transplantation (including CMV, EBV & BK infections)

P1-175 - Malignancies after renal transplantation in Korean recipients

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Background: With the number of kidney transplantations in Korea doubling, about 2300 cases in 2019, interest in long-term complications in transplant recipients is also increasing. Malignancy is one of the leading causes of death in recipients and the use of immunosuppressants or cancer-causing virus infection is considered as risk factors. Also, in them, it is known that the distribution and risk factors of cancers are different from those of the general population. So here we reported prevalence and risk factors of cancers in Korean kidney transplant recipients.
Methods: Using data from Korean National Health Insurance Service, we compared incidence of malignancies after renal transplantation to general population by standardizeds incidence ratios (SIR).
Results: Total 18854 (male:female 11173:7681, median age 47) patients were transplanted from 2003 to 2019, of which 1055 (5.6%) developed cancers. Compared to general population, recipients had 2 fold higher risk (SIR 2.23, 95% confidence intervals (CI) 2.1-2.37). In adults, highest risk cancer than general population is kaposi sarcoma (SIR 194.64, 95% CI 108.94-321.03) followed by non-melanoma skin cancer (SIR 10.05, 95% CI 7.72-12.86), kidney and other urological cancer (C64-68, SIR 8.8, 95% CI 7.57-10.18), and non-hodgkin lymphoma (SIR 8.01, 95% CI 6.28-10.07). Of 592 patients, under 19 years old, 23 (3.9%, SIR 31.85, 95% CI 20.19-47.79) developed cancer, of which 17(SIR 186.55, 95% CI 108.67-298.69) were non-hodgkin lymphoma. Cancer incidence was the lowest within 1 year after transplantation (133 of 1055, SIR 1.64, 95% CI 1.38-1.95), the highest after 1-3 years of transplantation (230 of 922, SIR 1.75, 95% CI 1.53-1.99), and thereafter gradually decreased.
Conclusion: Cancer risk after renal transplantation is higher than general population especially under 19 years old. Also, as types of cancer are different from general population, close monitoring and screening is necessary in transplant recipients.

Transplantation (including CMV, EBV & BK infections)

P1-176 - Recurrent Anemia in a pediatric kidney transplant recipient due to Parvovirus-B19. How many episodes can be posible?

Diego Morante[1], Laura Garcia Espinosa[1], Alejandro Zarauza Santoveña[1], Carlota Fernández Camblor[1], Juan Bravo Feito[1], Marta Melgosa Hijosa[1]
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Introduction: Parvovirus-B19 infection is a known cause of severe anemia in kidney transplant patients. Recurrences are unusual and imply a therapeutic challenge.
Case report: A 3-year-old male patient carrying his first living-donor kidney transplant (underlying disease Brachiootorenal syndrome) presented 2 months after transplantation symptomatic anemia requiring blood transfusion. The etiological study showed primoinfection with parvovirus B19 Polymerase Chain Reaction (PCR) and inmunoglobuline-M (IgM) positive. His baseline immunosuppressive treatment steroids, tacrolimus and mycophenolate-mofetil (MMF) was modified and mycophenolate-mofetil was temporarily suspended, with rapid remission. A new anemic episode 6 months later was treated with immunoglobulins (2g/kg total dose). Despite adjustments in immunosuppression, he presented 3 more episodes (16, 24 and 40 months post-transplant), requiring again blood transfusions and treatment with immunoglobulins. After the second recurrence MMF was replaced by rapamycin and after the last one rapamycin was discontinued keeping bitherapy with tacrolimus and steroids. PCR and immunoglobulin-M remained persistently positive and did not become negative until 4 years after the last recurrence. Mycophenolate-mofetil was restarted 1 year after PCR was negative, without new recurrences. At the present time, 10 years after transplantation, the patient has been 6 years without recurrences and remains asymptomatic with stable renal function.
Discussion: Recurrent anemic episodes secondary to parvovirus-B19 are exceptional and can have serious consequences. Their definitive management is controversial. Immunoglobulins are the treatment for each episode and their periodic prophylactic infusion has been proposed. Several schemes have been suggested to reduce immunosuppression without clear consensus. The persistence of PCR and positive IgM for long periods of time without negativization between episodes has been described, which makes management difficult.
Conclusion: Recurrence of parvovirus-B19 anemia on more than two occasions is exceptional. In these cases, PCR and IgM remain persistently positive even in absence of clinical manifestations. Treatment is based on immunoglobulins and reduction of immunosuppression.

Transplantation (including CMV, EBV & BK infections)

P1-177 - Acute antibody-mediated rejection concurrent with polyomavirus nephropathy in a transplanted patient with negative viremias. Is this possible?

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Introduction: The coexistence of acute humoral rejection and nephropathy secondary to polyomavirus in a patient with a kidney transplant is an uncommon finding in standard practice, and its therapeutic management remains a challenge. The unexpected finding of JC polyomavirus nephropathy impedes the diagnosis and following therapeutic approach.
Case report: A 17-year-old male teenager carrying their first living-donor kidney graft after 3 years presents worsening of renal function with serum creatinine increased to 1.8 mg/dl. He associated Class II anti-HLA donor specificity antibodies and a previous history of inmunosuppresion fluctuant levels. Viremia tests systematically performed for polyomavirus-BK during the previous follow-up were negative. A biopsy is performed observing results compatible with polyomavirus nephropathy and concurrent acute antibody-mediated rejection. Due to the persistently negative viremia and viruria, we established the possibility of another type of polyomavirus, as the etiological agent, detecting JC virus it in the patient's urine.
The coexistence of both entities requires an intricated therapeutical approach, in order to maintain the balance between minimizing immunosuppression to treat infection without increased renal harm due to humoral rejection. For our patient, an endovenous immunoglobulin treatment (2 g/kg) and changes on their base immunosuppression were performed, replacing mycophenolate with rapamycin and maintaining previous treatment with tacrolimus and increasing steroid dosage.
Renal function improved rapidly and remains stable one year after diagnosis and subsequent treatment. No anti-HLA antibodies have been detected during follow-up.
Conclusion: Although in most cases of nephropathy secondary to polyomavirus, the causal agent is the BK virus. The presence of a compatible biopsy with negative viremia and viruria requires ruling out the presence of JC polyomavirus. The simultaneous presence of this entity and acute humoral rejection is exceptional, poor treatment compliance seems to be the main risk factor. The initial treatment remains unclear and should be tailored to each patient.

Transplantation (including CMV, EBV & BK infections)

P1-178 - Evaluation of height, weight and body mass index of pediatric patients undergoing kidney transplantation and its correlation with epidemiological, laboratory and medication factors

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Introduction: Studies on the growth of pediatric patients after PKTx are difficult. This study aimed to assess the weight, height and body mass index (BMI) of PKTx and correlate the variations found with the epidemiological, laboratory and drug factors in this population, in a single reference center.
Patients and methods: Sixty-one PKtx (0–17yr and 11mo) were performed from January 2011 to January 2020. Weight gain, height and BMI in 1yr were correlated with gender, age, cause of ESRD, type of renal therapy before PKTx, type of donor, cold ischemia time (CIT), delayed graft dysfunction (DGF), type of induction and maintenance immunosuppression, rejection, glomerular filtration rate (GFR), CMV infection, graft loss and laboratory variables. The Shapiro Wilk test and the Wilcoxon test were used.

Results: The median age at transplant was 12yr. Males were predominant as well as the glomerular diseases as a cause of renal loss function, and of hemodialysis (HD) as pre-transplant therapy. Donation by deceased donor occurred in more than 98% and the median CIT was 13hr. Induction immunosuppression (ISS) with thymoglobulin (62.3%) and maintenance with tacrolimus (82%) and azathioprine (54%) were predominant. 36% of patients had DGF. The GFR had a median of 69.2ml (23.9-145.9ml) after 1yr of transplantation, graft loss occurred in six patients and death in only one. There were no relevant changes in laboratory tests. Multiple linear regression showed that the greatest height recovery was related to GFR and the patient's age at the time of transplantation. The greatest weight recovery was related to GFR and BMI for females and the absence of graft loss.
Conclusion: The study found correlations consistent with the literature (factors that interfere: height, weight and BMI). However, due to the short evaluation period and the small number of participants, it was not possible to confirm all the correlations.

Transplantation (including CMV, EBV & BK infections)

P1-179 - Seroconversion rates to SARS-CoV-2 mRNA vaccination in paediatric kidney transplant recipients

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COVID-19 mRNA vaccinations have been proven to be safe and effective in lowering the rates of COVID-19 related deaths and ICU admissions among affected individuals. Adult kidney transplant (KT) recipients have lower rates of seroconversion following full course of immunisation, when compared to immunocompetent individuals.
Aim: The primary aim of the study was to assess seroconversion rates following a standard two-dose schedule of SARS-CoV-2 mRNA vaccination in paediatric KT recipients. Secondary aims included assessing seroconversion rates following third dose of vaccine and identifying factors that impact response to vaccine.
Methods: 46 paediatric KT recipients aged 12-18 received SARS-CoV-2 mRNA vaccination as per local protocol at a single paediatric centre. SARS-CoV-2 serum immunoglobulin G (IgG) was analysed utilising the Vidas® enzyme linked immunofluorescence assay in a 6- 8-week window post second and third dose of immunisation. Demographic data including age, gender, time from transplant, deceased versus living related transplant, maintenance and induction immunosuppression and additional immune modulating therapies [including rituximab, IVIG, anti-thymocyte globulin (ATG) and tocilizumab] was collected.
Results: 21 patients were eligible for the study. Seroconversion rate after two doses of mRNA vaccination was 58% and it increased to 76% after a third dose. Two individuals were assessed only after their third vaccine and demonstrated positive IgG. Age, sex, underlying disease, type and time since transplant and other immune modulating therapies did not impact seroconversion rates. When compared with azathioprine, mycophenolate mofetil (MMF) was associated with poor vaccine response (p value = 0.012) as were increases in prednisolone dose by 0.01mg/kg/day (OR 1.60 95% CI1.02 to 2.54).
Conclusions: Seroconversion rate to SARS-CoV-2 mRNA vaccine in paediatric KT recipients following a two, and three dose vaccination schedule was 58%, and 76% respectively. MMF use and increasing increments in prednisolone dose of 0.01mg/kg/day were associated with poor seroconversion rates.

Transplantation (including CMV, EBV & BK infections)

P1-180 - Incidence of post-transplant lymphoproliferative disease after pediatric solid organ transplantation with use of induction immunosuppression

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Background: Post-transplant lymphoproliferative disease (PTLD) is a serious complication of solid organ transplant (SOT). The PTLD risk associated with induction immunosuppression in pediatric SOT recipients in the modern era of immunosuppression has not been quantified.
Methods: A single-centre, retrospective cohort study of SOT recipients < 18-years of age between January 1, 2002 and December 31, 2015. Episodes of PTLD identified by biopsy were classified using the 2016 WHO classification. Induction was defined as receiving anti-thymocyte globulin (ATG) and/or an interleukin (IL-2) antagonist within 7 days of transplant.
Results: A total of 769 children were transplanted (273 liver, 262 kidney, 181 heart, 38 Lung, 15 small bowel or multi-organ) with a follow up duration of 3384 person-years. Nighty-six episodes of PTLD occurred in 81 patients. Seventy-four (78%) PTLD cases were EBV positive. Overall PTLD incidence rate was 23.9 per 1000 person-years. Incidence rates were highest in lung and multi-organ transplants at 94.8 and 156.1 cases per 1000 person-years and lowest in kidney recipients at 10.7 cases per 1000 person-years. Medication data were available for 662 patients, 113 patients received induction with ATG, 293 an IL-2 inhibitor and 19 received both ATG and an IL-2. PTLD incidence rates were similar across induction groups (Table 1). Incidence rate ratios showed no difference in rates of PTLD by type of induction nor differs by PTLD subtype.

Table 1. Incidence and incidence rate ratio of PTLD overall and subtypes by induction type

	Incidence rate per 1000 person-yrs.		Incidence rate ratio
	IL-2 antagonist	ATG	ATG versus IL-2
All PTLD	33.3	33.2	1.00 (0.45 to 2.50)
WHO Class			
Early	16.7	16.0	0.90 (0.29 to 3.74)
Polymorphic	4.2	6.0	1.45 (0.18 to 66.81)
Monomorphic/ Hodgkin's lymphoma	1.3	1.1	0.88 (0.23 to 4.93)

Abbrev. PTLD, post-transplant lymphoproliferative disease; IL-2, interleukin- 2; ATG, anti-thymocyte globulin; WHO, World Health Organization.

Conclusion: The PTLD incidence rate was high, however, even those with early disease treated by adenoidectomy were included, and a significant number of multiple-organ, lung and small bowel recipients were included in the cohort, who are known to be at high risk. The PTLD incidence rate was not increased in children receiving induction with ATG compared to those receiving an IL-2 antagonist.

Transplantation (including CMV, EBV & BK infections)

P1-181 - Can complement pro-inflammatory and inhibitory factors in the biopsies of paediatric kidney transplant recipients (pKTR) predict prognosis?

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Background: The accurate and prompt diagnosis of antibody-mediated rejection (ABMR) in paediatric kidney transplant recipients (pKTR) is vital in allowing the early initiation of treatment to prevent renal allograft dysfunction and loss. The important role of complement activation in renal transplant immunology and rejection has been described, especially when some pKTR can have circulating peripheral donor specific antibodies for years. There are limited data in the paediatric population identifying the presence and deposition of specific complement pro-inflammatory and inhibitory factors in suspected ABMR.
Methods: Retrospective, single-centre study of percutaneous renal transplant biopsies from 10 pKTR with donor-specific antibodies (DSA) and a histological diagnosis of ABMR, were retrieved for immunohistochemistry (IHC) staining between April 2017 and September 2017. The cases were reviewed for the expression of complement induced pro-inflammatory (SYK, C3D) and inhibitory (CD46, CD55, CD59) factors.
Results: CD59 staining was positive in all 10 biopsies with stronger staining in the peritubular capillaries and patchy staining in the proximal and distal tubules, without evidence of CD55 staining. C3D staining showed predominantly strongly positive staining in glomerular capillaries, and occasional patchy staining in the tubules. SYK staining was patchy and confined to the distal tubules. CD46 showed mainly patchy staining in the basement membrane and occasionally patchy staining in the proximal and distal tubules.
Conclusions: Our study shows the important role of complement regulating proteins as biomarkers in ABMR. Positive CD59, C3D, SYK and CD46 staining was observed in biopsies of pKTR with ABMR, with varying strength and localisation. Further studies are warranted to evaluate their use as diagnostic and prognostic tools in ABMR, and to determine the potential role for complement targeted therapies.

Transplantation (including CMV, EBV & BK infections)

P1-182 - Treating refractory disseminated EBV associated post-transplant lymphoproliferative disease – Role of CTLs

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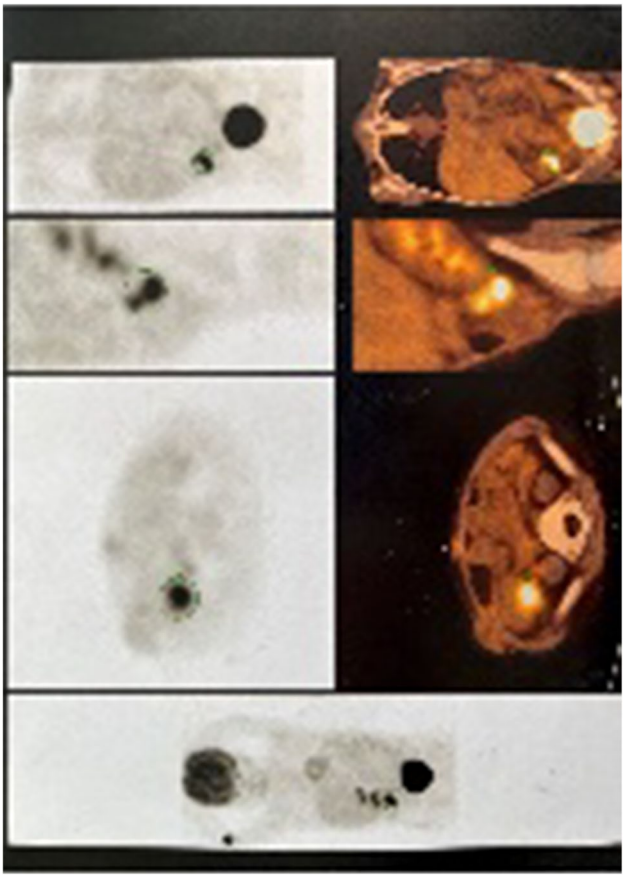
Background: Post-transplant lymphoproliferative disorder (PTLD) secondary to Epstein Barr Virus (EBV) infection in solid organ transplant recipients, even though rare, has very high mortality rate. The novel concept of adoptive immunotherapy in the form of EBV-directed cytotoxic T lymphocytes (CTLs) following reduction of immunosuppression, is a promising option in the treatment algorithm for management of PTLD. We report herein the first pediatric case of such treatment.
Case report: 6.5 year-old kidney transplant recipient, developed PTLD in the 3rd year post-transplant, in absence of EBV mismatch. The monoclonal gastrointestinal T and B-cell PTLD with leiomyoma, with initial focus at the appendix, caecum and terminal ileum, gradually spread to the lungs, spleen and the renal graft. Failure of response to the first line management, rituximab and intensive chemotherapy paved way to an open labelled trial for treatment with three alloreactive EBV directed cytotoxic T-cells infusions (5 x 10^6cells/kg/dose). Within the first two doses, the tumor regressed from all the sites. But it finally took over 2 years after the third dose, for the EBV-PCR to become non detectable. At last follow-up, after 10 years of her PTLD, she survives lymphoma-free.
Discussion/conclusions: EBV-directed cytotoxic T-lymphocyte (ex-vivo) infusions for treatment of PTLD in solid organ recipients are scarcely reported in adults. Generally incorporated once the disease reaches a more grave stage, i.e. after the failure of the first line treatment. We present herein the first pediatric case with a successful long-term outcome of 10 years after a trial of allogeneic CTLs in a very difficult to treat, severe and widespread polymorphic gastrointestinal PTLD after kidney transplantation. In lieu to the minimal adverse events without residual toxicity, this novel treatment might pave way to further trials considering this treatment modality alongside the cytotoxic chemotherapy.
Key words: Post-transplant lymphoproliferative disease, Epstein-Barr virus, Leiomyoma, EBV directed Cytotoxic-T lymphocytes



Transplantation (including CMV, EBV & BK infections)

P1-183 - Case Report: Primary lacrimal gland lymphoma - A rare presentation after pediatric kidney transplantation.

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Objective: Post-transplantation lymphoproliferative disease (PTLD) is the most frequent early malignant complication after pediatric kidney transplantation. It is a consequence of the uncontrolled proliferation of lymphocytes in the immunosuppressed patient. PTLD involvement of ocular and ocular annexa is very rare and is limited to a few cases in the literature. To the best of our knowledge, this is the first report of primary lymphoma in the lacrimal gland after pediatric transplantation.
Results: Girl, 10 years old, diagnosed with sacral myelomeningocele corrected shortly after birth and hydrocephaly treated with a ventriculoperitoneal shunt at 5 days of life. She underwent a deceased donor kidney transplantation after 18 months of hemodialysis. Her pre-transplant serology was positive for Epstein-Barr virus (EBV). After 4 years of transplantation, she developed a progressively increased nodule in the right upper eyelid, associated with local edema and eyelid ptosis. Visual acuity remained preserved (FIGURE). The investigation revealed a positive PCR for EBV and a biopsy of the left lacrimal gland revealed a monomorphic large B-cell lymphoma, CD20+, and the in-situ hybridization was EBV positive. The proposed treatment was immunosuppression withdrawal, associated with Rituximab and Cyclophosphamide chemotherapy protocol. There was clinical improvement soon after the first cycle of medication and throughout the treatment, the child had stable renal function (eGFR > 60ml/min/1.73m²).
Conclusions: PTLD can bring devastating consequences for the graft and for the patient life, with lymph node involvement as the most common PTLD presentation in children. Ocular PTLD is very rare, and only 2 cases in adult kidney transplant patients had been described. The diversity of body areas in which PTLD can develop implies that a high degree of diagnostic suspicion should be maintained to guarantee a rapid and efficient therapy.

Transplantation (including CMV, EBV & BK infections)

P1-184 - Epstein Barr Virus (EBV)- associated to Smooth Muscle Tumor (SMT) in a renal transplant recipient: Case Report.

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EBV is associated with malignancies in patients with immune impairment, even though EBV-SMT is a uncommon one. We report the case of 5 years old girl, with ESRD secondary to a nephrotic syndrome (WT1 mutation). At 3,5 years old, she received a renal transplant. Induction with Basiliximab and maintenance: prednisone, MMF and tacrolimus. She had a good outcome. By the time of transplantation she was CMV and EBV negative. 18 month post transplanted, she presented a tongue mass, plasma EBV -PCR was negative. She went into surgery. Histopathology suggested EBV-SMT. Stained positive for muscle cells,EBV PCR immunohistochemistry and in situ hybridization positive The tongue tumor recurred twice, and patient went into surgery again. Patient went into PET-SCAN that showed activity in lung, liver, spleen, kidney, and neck. Chest, abdomen and pelvis CT scan showed numerous masses in lung, liver, spleen and kidney. Because of the multifocal lesions, complete resection was not possible, hepatic and pulmonary biopsy were obtained and histopathology was consistent for SMT. The patient discontinued tacrolimus and mycophenolate and sirolimus was added.
Because some data indicated that patients CARMIL2- deficiency may have EBV-SMT at LMU Klinikum whole exome sequencing was performed for the patient, parents and brother. WT1 heterozigous variant as a novo event was found, but they could not identify significant sequence variants that could explain Human Inborn Errors of immunity. Finally, immune phenotyping by flow cytometry was informed as normal. After 18 months, of the diagnosis new lesions

in her tongue, has not appeared, renal function remains stable, but CT scans shows not decreased in mass.
EBV-SMTs is a rare entity. The majority of them are associated with solid organ transplantation and HIV infection. Current treatment include surgical resection, minimizing immunosuppression and sirolimus but further research is needed to establish the response to new treatments

Transplantation (including CMV, EBV & BK infections)

P1-185 - Disparities in treatment and outcome of kidney replacement therapy in children with comorbidities: An ESPN/ERA-EDTA Registry study

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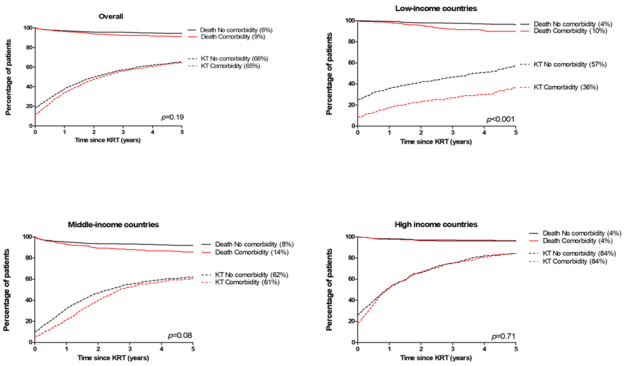
Background: Data on extra-renal comorbidities in children on kidney replacement therapy (KRT) is scarce. Considering its high relevance for prognosis and clinical decision-making, this study aims to analyse the prevalence of comorbidities in European children on KRT and its impact on outcome and access to kidney transplantation (KT).
Methods: We included data from patients aged <20 years when commencing KRT from 2007 to 2017 from 22 European countries included in the ESPN/ERA-EDTA Registry. Comorbidities were registered at the start of KRT. Differences in access to KT, patient and graft survival were estimated using Cox proportional hazard regression.
Results: At least one comorbidity was present in one third (33%) of the 4127 children commencing KRT, and acquired cardiovascular diseases occurred most frequently. The comorbidity prevalence has steadily increased by 5% per year since 2007. Comorbidities were most frequent in patients from high-income countries (43% vs. 24% in low-income and 32.9 in middle-income countries). Patients with comorbidities had a lower access to transplantation (aHR 0.67, 95% CI: 0.61 - 0.74), and a higher risk of death (aHR 1.79; 95% CI: 1.38–2.32). The increased risk of death was only seen in dialysis patients (aHR 1.60; 95% CI: 1.21-2.13), and not after kidney transplantation. For both outcomes, the impact of comorbidities was stronger in low-income countries (Figure 1). However, once transplanted, 5-year graft survival was not affected by the presence of comorbidities (aHR for graft failure: 1.18, 95% CI: 0.84-1.65).
Conclusions: Extra-renal diseases have become more frequent in children and adolescents on KRT and reduce their access to kidney transplantation as well as survival, especially when remaining on dialysis. Kidney transplantation should be considered as treatment of choice in all pediatric KRT patients and efforts should be made to identify modifiable barriers to KT for children with comorbidities.

Picture 1: Cumulative incidence of KT vs death as competing event



Transplantation (including CMV, EBV & BK infections)

P1-186 - Changes in body mass parameters in a paediatric renal transplant population during and after different stages of social lockdown during the coronavirus pandemic.

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Background and aims: Renal transplant patients are at greater risk of cardiovascular disease than the general population. Excess weight is a significant risk factor for all patients, with weight gain post-transplant a particular concern. This study assesses if renal transplant patients gained excess weight during periods of restricted activity due to social lockdowns during the coronavirus pandemic.
Methods: This retrospective observational study of children attending the renal transplant clinic monitored changes in weight and body mass index over the first 12 months of the SARS-Cov-2 pandemic, during which multiple restrictions on socializing and school attendance occurred.
Further follow-up data for the 12 month period following relaxation of restrictions has been gathered and analysed.
Results: 46 post-kidney transplant patients at least 6 months post-transplant were included. 26 patients gained weight, 11 patients had stable weight and 9 lost weight. The mean weight z-score across the patient cohort increased from -0.053 at start of lockdown 1, to 0.132 4 months post-lockdown 1, increasing further to 0.196 after lockdown 2. Mean BMI z-score increased from 0.633 at onset of lockdown to 0.788 at end of lockdown 1. Following relaxation of restrictions, weight z-score and body mass index remained stable, but did not fall to pre-restriction levels.
Conclusion: The majority of paediatric post-kidney transplant patients demonstrated increases in weight and BMI z-score over the periods of lockdown, with this weight gain sustained after restrictions were eased. The potential consequences of the pandemic and societal responses continue to emerge.

Transplantation (including CMV, EBV & BK infections)

P1-187 - Graft loss in paediatric and young adult kidney transplantation in New Zealand: who is at greatest risk and when?

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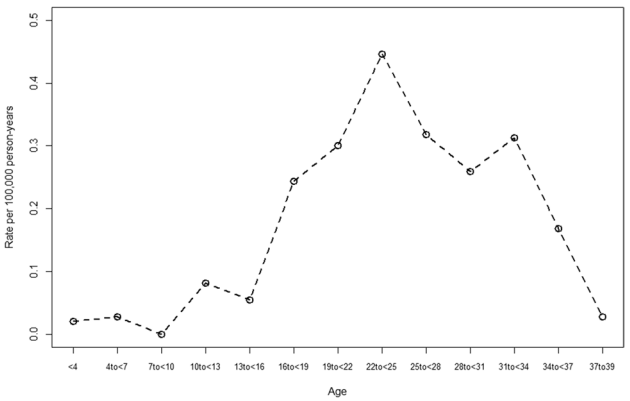
Introduction: Recipient age at time of kidney transplant (KT) is associated with graft survival and more recently, recipient age (irrespective of time post KT) has been associated with graft loss. We determine the rate of KT loss among children and young adults that were either transferred to adult medical services (PTA) versus receiving care under solely paediatric (PO) or adult services (AO).
Materials & methods: Retrospective review of all first KT recipients aged 0-24 years between 2000 - 2019 in NZ. Sample population and variables of interest were obtained from Australia and NZ Dialysis and Transplant Registry. Primary outcome was time to transplant loss. Follow-up was until graft loss, 40 years of age or end of study period, whichever was earliest. Confounder and effect modifier covariates were identified and studied using Cox proportional hazard models.
Results: 244 (PO=54, PTA=55, AO=135) KT events met inclusion criteria. Median follow-up was 7.3 years. Rates of graft loss were 17%, 36%, and 37% for the subgroups PO, PTA, and AO respectively. Crude age specific graft failure rates were highest for 22 to 24 year age bracket (1.4 per 100000 person years) with inferior outcomes starting from age 16, peaking at 24 and again at 32. For PTA subgroup, median age at transfer was 17.1 years (16.4-18.1), transplant duration at transfer was 5.2 years (2.2-8.5), time to graft loss after transfer was 4.6 years (1.9-6.0), with 27% of patients transferred to adult service losing their graft within 5 years.
Conclusions: Among first KT recipients, older adolescents and young adults have the highest rates of graft failure. The first five years after transfer from paediatric to adult services reflect a high-risk period. Comprehensive and coordinated adolescent and young adult care models are needed to mitigate this risk.



Transplantation (including CMV, EBV & BK infections)

P1-188 - Arterial stiffness and body composition in a racially diverse pediatric kidney transplant population

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Background: Kidney transplant recipients are at increased risk for obesity and cardiovascular (CV) disease. Studies have shown worse CV outcomes among African American and Hispanic recipients than Caucasians. Determinants of arterial stiffness and body composition in racially diverse pediatric kidney transplant recipients are not well known.
Methods: We conducted a cross-sectional study of 56 kidney transplant recipients 6-21 years of age and ≥ 6 months post-transplant. Augmentation index adjusted at heart rate 75 bpm (AI) and pulse wave velocity (PWV) were measured oscillometrically (Mobilograph). BMI and percent body fat (PBF) were evaluated using bioelectrical impedance analysis. Participants completed the Perceptions of Racism in Children and Youth (PRaCY) questionnaire, a validated measure of perceptions of racism and discrimination.
Results: Participants (57% male, median age 14 years) were racially/ethnically diverse (18% White, 32% African American, 41% Hispanic, 9% other races). 49% of patients had high PWV (≥90^{th} percentile-for-age-and-height). Median AI was 27.0 (normal 22.2). PBF was 21.7% in males and 36.1% in females (normal 16.6% and 24%, respectively). BMI z-score was 0.59. A subset of 31 participants completed PRaCY; of these, 9 (29%) had high perception of racism. Multivariable analysis adjusted for age and sex showed BMI (β2.4, p 0.01) and Hispanic race (β6.2, p 0.005) independently associated with increased arterial stiffness (AI). History of any dialysis prior to transplant was associated with high PWV post-transplant (OR 6.4, p 0.03). High perception of racism was associated with higher PBF (OR 1.5, p 0.04) adjusted for BMI, age and sex.
Conclusions: Arterial stiffness is common in pediatric kidney transplant recipients, particularly those with higher BMI, exposure to dialysis prior to transplant, and Hispanic ethnicity. Greater exposure to racism is associated with higher percent body fat, regardless of BMI. Further research is needed to elucidate how racism impacts metabolic and cardiovascular outcomes long-term.

Transplantation (including CMV, EBV & BK infections)

P1-190 - BK Virus Infection and Mycophenolate Mofetil Exposure in Pediatric Kidney Transplant Recipients.

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Background: BK polyomavirus (BKPyV) is an important cause of kidney allograft dysfunction. Mycophenolate mofetil (MMF) has been identified as one the risk factors for BKPyV. MMF exposure with an area under the concentration time curve (AUC) 30- 60 mg h/L is an established target to prevent rejection. However, the effect of this level of exposure on the incidence of BKPyV infection in children is unknown. The aim of this study was to examine the effect of the exposure of MMF on BKPyV in pediatric kidney transplant recipients.
Design: Single center, retrospective study of pediatric kidney transplant recipients between 2010-2019. BKPyV infection included BK viruria (BK), BK viremia (BKV), and BK nephropathy (PyVAN) during the initial post-transplant year. Mycophenolic acid (MPA) levels were measured at 1,6- and

12-months. Chi-square/Fisher's exact tests and Wilcoxon Rank Sum tests were used to compare categorical and continuous variables respectively.
Results: 115 patients were included, of which 40 (35%) had BK, 26 (22%) BKV, and 6 (5%) PyVAN. There was no significant difference in age, sex, etiology of end stage kidney disease, or cold ischemia time between the BK + and the BK - group. Risk factors associated with BKV in univariate analysis was the presence of rejection (59% vs 28%, p= 0.003) and younger age (8 years vs 12 years, p= 0.024). There was no difference in the median MMF AUC levels between the BK+ and BK- group (48.6 mg h/L vs 42.9 mg h/L, p = 0.5943). There was no significant difference in the proportion of subjects who had BK infection at median AUC values < 30 mg h/L (4/30, 13%), 30-60 mg h/L (20/59, 66%), > 60 mg h/L (6/19, 20%, p = 0.900).
Conclusion: Our study did not identify an association between MMF exposure and BKV infection in pediatric kidney transplant recipients.

Transplantation (including CMV, EBV & BK infections)

P1-191 - Tacrolimus intra-patient variability and its effect on acute rejection, graft function and development of donor specific antibodies in paediatric kidney transplant recipients

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Background: Adequate immunosuppression is essential for long term graft outcomes after kidney transplantation (KT). Intra-patient variability (IPV) in tacrolimus trough levels (TTL) has been associated with increased rejection, graft loss, and de novo donor-specific antibody (dnDSA) development in KT recipients. This study investigated the effect of tacrolimus IPV on paediatric KT outcomes. METHODS: This retrospective cohort study evaluated paediatric KT recipients at a single centre; The Children's Hospital at Westmead. We collected TTL and calculated coefficient of variance (CV = SD/mean x 100) during post KT years 1-5 and examined its association with acute rejection and development of dnDSA. Patients who experienced acute rejection or developed dnDSA within 12 months were excluded from analysis. RESULTS: A total of 30 paediatric KT recipients (16 males; 54%) with a mean age of 6.0 ± 4.0 years were included. Of 28 patients, acute graft rejection occurred in 6 patients (21.4%). The mean tacrolimus CV was 43.7% ± 18.6% compared to 29.9% ± 8.1% in patients who did have any episodes of acute rejection. Of 27 patients who were tested for de novo donor specific antibodies, they were detected in 13 (48.1%). The mean tacrolimus CV was 35.7% ± 15.8% compared to 28.1% ± 8.3% in patients who did not develop donor specific antibodies. CONCLUSION: Acute rejection and development of donor specific antibodies in paediatric kidney transplant recipients appears to be associated with increased levels of tacrolimus IPV.

Transplantation (including CMV, EBV & BK infections)

P1-192 - Association of rapid weight gain following renal transplantation and development of obesity and hypertension: an analysis of the North American Pediatric Renal Trials and Collaborative Studies registry

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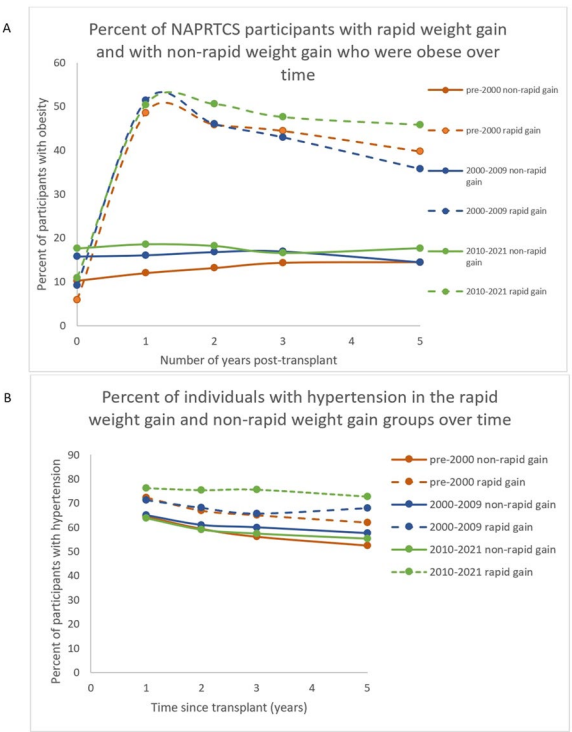
Introduction: Cardiovascular disease remains a leading cause of morbidity among children with kidney transplants. We evaluated whether there was an association between rapid weight gain (RWG) in the first year following transplantation and development of obesity and hypertension among children enrolled in the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) registry.
Methods: This was a retrospective analysis of the NAPRTCS transplant cohort; we assessed for RWG in the first year post transplant, defined as an increase in BMI% of greater than 20 within one year of transplant, and evaluated obesity and hypertension in children with and without RWG up to 5 years post-transplant. We evaluated three separate eras based on the time of first transplant (pre-2000, 2000-2009, and 2010-2021). We performed chi square analyses and logistic regression analyses to assess cardiometabolic risk factors and RWG in the first year after kidney transplantation adjusting for sex, age, race, and time from transplant.
Results: The percent of children with RWG decreased across the 3 eras (pre-2000 37.3%, 2000-2009 23.0%, 2010-2021 12.9%). Obesity was significantly more common among children with a history of RWG following transplant, and persisted at 5 years following transplant, with 35-45% of children with RWG having obesity 5 years following transplant compared with 14-17% of children without RWG. Hypertension was also significantly more common in the group with RWG than the group without RWG at all but 3 time points. The odds of obesity in the RWG group compared with non-RWG was 2.2 (95% CI: 1.99-2.5), and the odds of hypertension was 1.06 (95% CI: 1.01-1.13).
Conclusions: RWG was significantly associated with both obesity and hypertension among pediatric renal transplant recipients enrolled in NAPRTCS. Interventions targeting RWG following renal transplant should be evaluated as a potential way to improve cardiovascular outcomes in this population.

Figure 1: Obesity (panel A) and hypertension (panel B) over time among children with and without RWG



Transplantation (including CMV, EBV & BK infections)

P1-193 - What are the challenges of kidney transplantation in children weighing less than 15 kg?

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Objective: Kidney Transplantation (KT) in infants has technical challenges and may be associated with higher complication rates and lower graft survival than in older patients. This study compares a single-center results of KT recipients weighing <15 kg to those ≥15 kg.
Methods: Charts were reviewed for KT recipients from January 2008-December 2020. Two groups were created: one with all recipients <15 kg, and a comparison group of an equal number of recipients ≥15kg who were matched according to when the transplant was done.
Results (Table1): There were 88 patients in total: 44 in each group. There was no difference in the rate of dialysis at transplant between the two groups (Table1). Living donors were used significantly more often in the <15 kg group (64% vs 30%, p<0.001). Intraperitoneal transplants were significantly more common in the <15kg group (95% vs 11%). Vascular complications were low in both groups and not significantly different (Table1). Cold ischemia time was shorter in the <15kg group (6.1 vs 9.1 hours, p=0.003), but total OR time was significantly longer (4.2 vs 3.4 hours, p<0.001). The <15 kg group had longer ICU and hospital stays and were longer to re-establish enteral feeds. Acute cellular rejection was more common in older children (48% vs 25%, p<0.05) There was a similar incidence of PTLD in both groups. One and five-year graft survival was almost identical in the two groups: <15 kg, 92% and 78%, ≥15kg 95% and 78%. Mean follow-up was 4.9 +/- 3.7 years.
Conclusions: Our results demonstrate that KT in patients <15 kg has outcomes similar to those in older children and should not be considered an impediment to timely transplantation.

	Total (N=88)	Under 15 kg (N=44)	Over 15 kg (N=44)	p-value
Age at Transplant (years), median (IQR)	5.5 (2.0, 14)	2.0 (1.6, 2.7)	13 (9.1, 16)	**<0.001**
Dialysis at Transplant, n (%) N=70	70 (80%)	37 (84%)	33 (75%)	0.29
Congenital Etiology of CKD, n (%)	54 (62%)	35 (80%)	19 (34%)	**<0.001**
Living Donor, n (%)	41 (47%)	28 (64%)	13 (30%)	**0.001**
Intraperitoneal Placement, n (%)	47 (53%)	42 (95%)	5 (11%)	**<0.001**
Cold Ischemia Time (hours), mean +/- SD	7.7 +/- 4.4	6.1 +/- 3.7	9.1 +/- 4.6	**0.003**
OR Time (hours), mean +/- SD	3.8 +/- 1.1	4.2 +/- 1.1	3.4 +/- 1.0	**<0.001**
Renal Artery Complications, n (%)	0	0	0	-
Renal Vein Complications, n (%)	1 (1.1%)	1 (2.3%)	0 (0%)	0.32
Other Return to OR, n (%)	9 (10%)	7 (16%)	2 (4.5%)	0.079
Hospital Days, mean +/- SD	21 +/- 21	27 +/- 27	14 +/- 10	**0.006**
Days to Enteral Feed, mean +/- SD	4.9 +/- 5.2	6.5 +/- 6.5	3.3 +/- 2.8	**0.004**
ICU Days, mean +/- SD	4.9 +/- 4.3	5.9 +/- 5.2	3.9 +/- 2.9	**0.029**
Patients with DGF, n (%)	10 (11%)	2 (4.5%)	8 (18%)	0.052
Patients with PTLD, n (%)	11 (13%)	7 (16%)	4 (9.1%)	0.334
Patients with an Acute Rejection, n (%)	32 (36%)	11 (25%)	21 (48%)	**0.037**
1-year Graft Survival, n (%) N=79	74 (94%)	36 (92%)	38 (95%)	0.623
5-year Graft Survival, n (%) N=41	32 (78%)	25 (78%)	24 (78%)	0.97
1-year Patient Survival, n (%) N=79	78 (99%)	38 (97%)	40 (100%)	0.308
5-year Patient Survival, n (%) N=38	35 (92%)	20 (87%)	15 (100%)	0.145

Table1: Demographics, complications, and outcomes of patients receiving Kidney Transplantation by weight group. Mean and SD given for parametric variables. Median and IQR given for non-parametric variables.

Transplantation (including CMV, EBV & BK infections)

P1-194 - National study on the risks of COVID-19 for paediatric renal transplant recipients

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Introduction: From the start of the COVID-19 pandemic, evidence emerged that children were less affected by SARS-CoV-2 PCR DNA COVID-19 positive infections, with increasing evidence showing immunosuppressed children were less at risk compared to immunosuppressed adults. The aim of our study was to investigate how COVID-19 infections affected paediatric renal transplant recipients in the UK.
Methods: Questionnaires regarding patient demographics, transplant information, COVID-19 infection data and care of patients during the COVID-19 pandemic were sent out to all 13 UK paediatric nephrology centres.
Results: 64 patients (72% male; 44% Black, Asian and minority ethnic [BAME]; 64% living donors) aged 4-19 (median 12) years and between 1 month – 15 years (median 3 years 1 month) post-transplantation from nine centres tested positive for SARS-CoV-2 PCR DNA. Four centres had no positive patients. 48% presented with the classical COVID-19 symptoms (36% fever, 17% continuous cough and 3% loss of sense of taste or smell); atypical presentations included diarrhoea (13%) and lethargy (13%). 31% of patients were asymptomatic. 28% were hospitalised (median stay 2 days) which included asymptomatic patients admitted for other reasons. Of those admitted, one patient required oxygen; however, no patients required ventilation or intensive care admission. One child had a rejection episode as a complication of the infection, another child developed transaminitis and one child was treated for PIMS-TS, although a diagnosis was never confirmed. There was evidence of AKI with renal transplant dysfunction in 31% of patients, with increase in mean baseline plasma creatinine from 79.6µmol/l to 168.6µmol/l, but no patients required CVVH or dialysis.
Conclusion: 10.4% of the UK paediatric renal transplantation population have had documented SARS-CoV-2 PCR DNA infections with 28% required hospitalisation. There was increased prevalence of AKI, particularly after the first wave of the COVID-19 pandemic, possibly due to different variants, although there is no specific virological data to support this.

Transplantation (including CMV, EBV & BK infections)

P1-195 - Serologic response to Coronavirus disease 2019 (COVID-19) infection and vaccination in pediatric kidney transplant recipients compared to healthy children

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Introduction: The clinical course of COVID-19 infection in pediatric kidney transplant recipients (KTR) is milder and their serologic response to the BNT162b2 mRNA vaccine is superior to adult KTR. The aim of our study is to compare the serologic response of naturally infected or vaccinated pediatric KTR to that of healthy controls.
Methods: The study group consisted of pediatric (age ≤ 18y) KTR and a control group of healthy children, with a previously confirmed COVID-19 infection, or having received two doses of the BNT162b2 mRNA vaccine. Serological response was measured by anti-spike protein IgG antibody titers. Serologic response post-booster vaccination was additionally assessed in pediatric KTR.
Results: Fourteen children in each group had a previously confirmed infection. All except one KTR had mild infection. Pediatric KTR were significantly older with higher antibody titer levels compared to controls [median (IQR) age: 14.9 (11.1, 17.4) vs. 6.3 (4.5, 11.5) years, p=0.02; median (IQR) titer: 1695 (982, 3520) vs. 716 (368, 976) AU/mL, p=0.03]. Twenty-four KTR and 28 controls were vaccinated. Eighteen (75%) of KTR became seropositive compared to 28 (100%) of controls (p=0.007). Antibody titer levels were significantly lower in KTR vs. controls [median (IQR): 803 (206, 1744) vs. 8023 (3032, 30,052) AU/mL, p<0.001]. Fourteen KTR received a booster vaccination, 4 patients did not seroconvert. Antibody titer post booster in KTR reached similar levels to those of controls post two doses [median (IQR) 5923 (2295, 12,278) vs. 8023 (3034, 30,052) AU/mL, p=0.37].
Conclusion: Serologic response to COVID-19 infection was significantly higher in KTR compared to controls, contrary to the expected given their immunosuppressed status. Antibody response was higher in response to infection vs. vaccination in KTR, opposite of what is reported in the general population. Response to vaccination was lower in KTR compared to controls, reaching comparable levels only after booster vaccination.

Urology (including UTIs, kidney stones and bladder dysfunction)
P1-196 - A study of association of Lower Urinary Tract Dysfunction with rectal distension in children

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Context: Bowel Bladder Dysfunction (BBD) is combination of one or more bowel symptoms associated with Lower Urinary Tract Symptoms (LUTS). Close anatomical proximity and common nerve supply may support association between constipation and Lower Urinary Tract Dysfunction (LUTD).
Aim: To study association of LUTD with rectal distension and constipation in 5-15 years children.
Study setting and design: Prospective observational study in tertiary level teaching hospital (October 2019 to April 2021).
Methods: Total 45 children with symptoms of LUTD (defined by International Continence Society) were enrolled and assessed for constipation using Bristol stool chart, ROME III criteria and transabdominal ultrasound for rectal diameter. Dysfunctional Voiding Symptom Scoring (DVSS) questionnaire was used for quantifying severity of LUTD. Response in symptoms of LUTD was assessed after 4 weeks of treatment for constipation and urotherapy.
Statistical Analysis used: SPSS version 21
Results: Mean age of subjects was 8.29±2.1 years (51.11% females, 48.99% males). We observed storage symptoms in 100%, voiding symptoms in 33.33%, holding maneuvers in 42.22 % and nocturnal enuresis in 64.44%. Constipation was present in 22(48.88%) patients. Organic etiology for LUTS was identified only in 8 (17.78%) patients (rest were functional, 82.2%). Higher DVSS score was significantly associated with constipation. DVSS score ≥6 was seen in 20 out of 23 females, out of which 13 (65%) had constipation(p=0.537). DVSS score ≥9 was seen in 7 male patients, out of which 5 had constipation(p=0.05). Rectal distension (>30mm) was present in 8 patients (17.78%). Mean rectal diameter was higher in constipated children (25.55±6.66 vs 21.47±5.15 in non-constipated, p=0.026). Rectal distension was significantly associated with organic causes (p=0.002). After 4 weeks of treatment, response (complete or partial) was seen in majority symptoms (urinary frequency-93.75%, urgency-92.59%, incontinence-83.33%, nocturnal enuresis-82.76%).
Conclusion: Children with LUTD should be evaluated and treated for constipation if present, to improve response rate.

Type of lower urinary tract dysfunction	No constipation (n=23)	Constipation (n =22)	Total	P value
Organic cause (8)	3 (37.50%)	5 (62.50%)	8 (100%)	0.459 †
Nocturnal enuresis (29)	14 (48.28%)	15 (51.75%)	29 (100%)	0.608
Overactive bladder (11)	5(45.45%)	6(54.55%)	11(100%)	0.666 ‡
Cystitis (6)	2(33.33%)	4(66.67%)	6(100%)	0.414 †
Voiding postponement (5)	3(60%)	2(40%)	5(100%)	1†
Giggle incontinence (2)	0(0%)	2(100%)	2(100%)	0.233 †
Dysfunctional voiding (2)	1(50%)	1(50%)	2(100%)	1†
Underactive bladder (1)	0(0%)	1(100%)	1(100%)	0.489 †
Extraordinary daytime urinary incontinence(1)	0(0%)	1(100%)	1(100%)	0.489 †

†Fisher's exact test, ‡Chi square test

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-197 - Urinary calcium/creatinine and citrate/creatinine ratios in assessing hypercalciuria and hypocitraturia in Canadian children seen in the nephrolithiasis clinic

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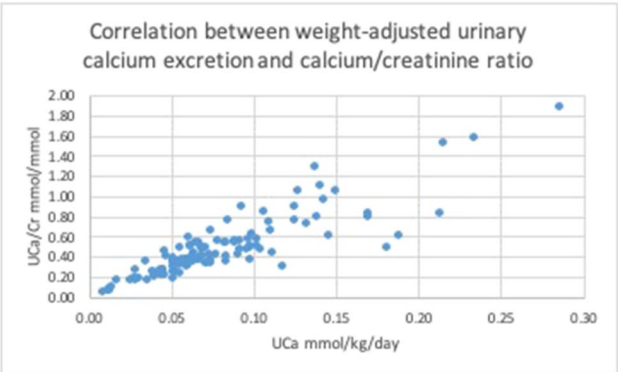
Introduction: There is an ongoing debate whether the urine calcium/creatinine ratio, which can be done on a spot urine sample, in clinic is a valid substitute for a full 24-hour urine collection to assess hypercalciuria. Currently, there is conflicting data from several other countries, but none from Canada.
Methods: Retrospective chart review analyzed data from a cohort of 130 patients who attended nephrolithiasis clinic and completed a 24-hour urine collection. 115 urine samples in 55 girls and 60 boys ages 4-18 were considered adequate based on urine creatinine excretion >0.1 mmol/kg/day. Pearson correlation was used to assess the relationships between urine calcium/creatinine ratio and urinary citrate/creatinine ratio versus the 24-hour urine calcium excretion (24UCa) and citrate (24UCit) of three different weight classes (<40 kg, 40.01 – 60 kg, >60.01 kg) and the entire cohort. Sensitivity and specificity values were established against the internationally accepted norms.
Results: Figure 1 shows a strong positive correlation between the urine calcium/creatinine ratio and weight adjusted 24UCa.



Pearson correlation coefficients between the urinary calcium/creatinine ratio and 24UCa for weight classes <40 kg, 40.01–60 kg, >60.01 kg, and entire cohort, showed values of 0.77, 0.88, 0.93, and 0.87 respectively. Sensitivity was 0.63, and specificity 0.89. Urinary citrate/creatinine ratio and weight adjusted 24-hour urine citrate Pearson coefficients for weight classes <40 kg, 40.01–60 kg, >60.01 kg, and entire cohort, showed values of 0.74, 0.93, 0.78, and 0.83 respectively.
Conclusion: Urine calcium/creatinine and citrate/creatinine ratios correlated well with total weight adjusted calcium and citrate excretions in the 24-hour urine collections. Good correlation was mainly seen in patients with normal 24UCa excretion. However, sensitivity of Ca/Cr ratio was moderate and unable to accurately predict hypercalciuria in around 40% of cases. Due to a lower calculated sensitivity, it could not be recommended to replace the 24-hour urine collection to detect hypercalciuria.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-198 - Nocturnal enuresis with overactive bladder is more prevalent than monosymptomatic nocturnal enuresis in pediatric patients

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Background: Nocturnal enuresis (NE) occurs when the amount of urine made during sleep exceeds bladder capacity and the individual does not awaken to the signal of a full bladder, resulting in involuntary emptying from reflexive bladder contraction. While difficult sleep arousal and nocturnal polyuria are major contributors to monosymptomatic NE (MNE), low bladder capacity from overactive bladder (OAB) and incomplete defecation (ID) are major contributors for non-MNE. This study reports the prevalence of OAB and ID in patients 5-21 years from 2007-April 2022 with NE occurring ≥1/week for ≥3 months.
Methods: Detailed history of diurnal and nocturnal voiding habits, defecation, and easy versus difficult sleep arousal was obtained. OAB was diagnosed if patients had ≥2 of the following ≥5 times/week: urinary urgency, urge incontinence, pelvic withholding maneuvers, and/or urinary hesitancy. ID was diagnosed if patients had wide stools, fecal smearing, and/or postponement of defecation ≥1/week in the previous 3 months.
Results: Of 959 patients with NE, 82% (782) manifested diurnal OAB and only 18% (177) had MNE. OAB accompanied NE in 77% of males and 85% of females. 54% of patients with MNE were male. OAB symptoms were elicited only on direct questioning or noticing signs of urinary incontinence on perineal examination in 40% of patients. ID was noted in 56% of NE patients with higher prevalence in NE with OAB versus MNE patients (65% versus 24%). ID data was only available for 253 patients. Nocturia and easy sleep arousal were more prevalent in patients with NE with OAB versus MNE.
Conclusions: NE with OAB is more prevalent than MNE. OAB symptoms can be missed on a cursory history and examination. The implication of this finding is that treatment of NE with OAB should address and manage OAB, while addressing difficult sleep arousal and/or nocturnal polyuria is important for MNE.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-199 - Antibiotic susceptibility to the causative microorganisms of childhood acute urinary tract infection; a following result after 10 years

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Urinary tract infection (UTI) is the most common bacterial disease and a common indication for antibiotic use in children. Because of the difficult in early diagnosis and rising resistance to antibiotics, the appropriate selection of antibiotics in treating bacterial UTIs is necessary to avoid the antibiotic overuse and misuse. The aim of this study was to compare the antibiotic susceptibility changes of UTIs with those before 10 years in Korea. We retrospectively identified the causative pathogens from these 571 samples and analyzed the change in antibiotics susceptibility compared to the previous our study.
Among culture (+) 571 UTI patients, 561 (98.2%) samples were Gram-negative strains: *E. coli* (89.1%), *Klebsiella* spp. (3.7%), *Enterobacter* spp. (3.0%), *Proteus* spp. (1.4%), etc. Among 509 patients with *E. coli* cultured, the antibiotic susceptibilities were as follows: imipenem, 100%; amikacin, 100%; gentamicin, 58.2%; cefepime, 95.3%; piperacillin/tazobactam, 93.7%; ceftazidime, 90.2%; aztreonam, 87.4%; ciprofloxacin, 83.9%; cefotaxime, 64.2%; amoxicillin/clavulanate, 58.2%; trimethoprim/sulfamethoxazole, 51.7%; and ampicillin, 21.0%. Comparing the differences in antibiotics susceptibility between

2003-2008 and 2015-2020, all bacteria (2003-2008, n=405; 2015-2020 n=558); antibiotics susceptibility was significantly decreased in 2015-2020 compared to 2003-2008 in the following antibiotics.; aztreonam 96.2%→87.1% (p<.001), cefazolin 81.15%→58.8% (p<.001), gentamicin 93.02→61.5% (p<.001), trimethoprim/sulfamethoxazole 71.8%→55.2% (p<.001), 3rd generation cephalosporin (2003-2008 ceftriaxone, 2015-2020 cefotaxime) 95.61%→66.1% (p<.001). ESBL-positive rates were 116 (20.3%) among all bacteria (n=571) and 112 (22.0%) among the *E. coli* (n=509), which were much higher than that reported among 2003-2008 data. We also found that vesicoureteral reflux was detected in 100 (21.6%) out of the 462 patients who underwent VCUG, and that the more severe grade of VUR, the higher antibiotics resistance.
In summary, we concluded that as the antibiotic resistance of bacteria causing UTIs increases in Korea as time goes by, it seems necessary to reconsider the selection of antibiotics in treating bacterial UTIs in antibiotics-overused community.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-200 - Primary Hyperoxaluria and Genetic Linkages: An insight into the disease burden from Pakistan

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Background and Objective: Autosomal recessive disorders are prevalent in Pakistan, a developing South Asian country where consanguineous marriages are common. This study seeks to determine the prevalence of monogenic causes in children presenting with nephrocalcinosis and nephrolithiasis at a dialysis and transplant centre in Karachi, Pakistan.
Methods: A retrospective study was conducted in children aged 1-18 years of age presenting with nephrocalcinosis, between 2010 and 2019. Demographic information was collected from caregivers, and clinical profile, laboratory parameters and stone analysis recorded on a pre-designed questionnaire. Next Generation Sequencing (NGS) was also performed to get molecular diagnosis of Primary Hyperoxaluria (PH).
Results: One hundred and twenty-six children were included, with 11 diagnosed as renal tubular acidosis, and 3 with Bartter's syndrome. Sixty-four percent were males. NGS and Sanger sequencing was performed on 112 children. History of parental consanguineous marriage was found in 98% of the cohort. Family history of stone disease was found in 34% of the cases. Forty-three percent and 32% presented with CKD Stage 1, and CKD Stage 5 respectively. Forty-one patients required dialysis at the time of presentation. Eighty-seven patients were diagnosed with PH, with mutations in AGXT gene found in 73, followed by GRHPR in 13, and HOGA in 1. Twenty-five patients reported negative for mutations.
Conclusions: Mutations noted in our cohort are different from those reported in the developed world. The disease poses a major disease burden in developing world context with the only treatment option of combined liver-kidney transplantation not available in Pakistan.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-201 - Temporary renal enlargement in children at the first episode of febrile urinary tract infection is a significant prognostic factor for vesicoureteral reflux

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Introduction: Morphological abnormalities of the kidney and urological system in children with febrile urinary tract infection (fUTI) are a predictive factor for long-term renal prognosis. However, no data are available on clinical characteristics and vesicoureteral reflux (VUR) related to sonographic temporary renal enlargement during the first fUTI episode, particularly regarding whether renal enlargement is temporary. Material & Methods: We conducted a multicenter cohort study of children who underwent renal ultrasound during their first fUTI episode between 2013–2020 and who were aged <7 years at diagnosis. Sonographic temporary renal enlargement was defined as increased renal length during the acute phase of fUTI following normal renal length after antibiotic treatment. We have a policy of administering voiding cystourethrography (VCUG) to children with fUTI and grade 2 hydronephrosis, microorganisms other than *Escherichia coli* in urine culture, renal deterioration, hematuria during initial fUTI episodes, and recurrence of fUTI after completing antibiotic therapy for initial fUTI. Results: This study included 343 children (237 boys), and mean age at diagnosis of fUTI was 0.55 ± 0.89 years. Thirty-six children had sonographic temporary renal enlargement at the first episode of fUTI. In children with temporary renal enlargement, serum CRP levels were significantly higher, and total duration of fever during their first fUTI was significantly longer than those without temporary renal enlargement. Additional analysis of 100 children receiving VCUG in accordance with our policy showed the proportion of children with VUR in the renal enlargement group was significantly higher than those in the nonrenal enlargement group (14/16; 88% vs 46/84; 55%, p=0.02). Nine of 14 children with VUR (64 %) received VCUG because of recurrence of fUTI. Conclusions: Our results suggest that the new policies for VCUG dependent on whether children at the first episode of fUTI have sonographic temporary renal enlargement can be recommended.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-202 - Fragile Bones in 18-35 year old with Crohn's Disease and Kidney Stones

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The aim of the study is to explore the prevalence of osteoporosis (OP) in patients with Crohn's disease (CD) and kidney stones (KS).
A retrospective large-scale bioinformatics database, Information for Integrated Biology and Bedside depository data (i2b2) of the UF Health System was used to analyze the prevalence of osteoporosis in CD patients with KS and the general population from November 2011 to September 2017. The i2b2 repository database runs systematic query searches based on ICD and CPT codes used for institutional billing. Statistical analysis was performed using the SASv. 9.4 software.
The total population was 1,002,357, ages 18-95 years old were 83,2910. Males 18-95 years were 44.7%. In the general population, the prevalence of osteoporosis was 0.19%, 0.27%, 0.44%, 0.68%, 0.86%, 1.06%, 1.67% in males and 0.20%, 0.39%,0.93%, 2.55%, 5.11%, 6.70%, 9.16% females in the age groups 18-34, 35-44, 45-54, 55-64, 65-74, 75-84, >85 respectively. In the Crohn's disease with kidney stones cohort, the prevalence of osteoporosis was 11.1%, 0%, 0%, 27.8%, 10.6%, 15.4%, 0% in males and 13.6%, 0%, 24%, 26.2%, 41.7%, 44.4%, 0% in females in the age groups 18-34, 35-44, 45-54, 55-64, 65-74, 75-84, >85 respectively. No patients or 0% of patient indicated osteoporosis, but did not exclude osteopenia. The prevalence of osteoporosis in the CD with KS cohort was higher in the 18-35 year old group compared to the 85-95 year old general population in males: 11.1% vs. 1.67%($p<0.001$) and females: 13.6% vs. 9.16%($p<0.001$).
The rate of OP in patients with CD and KS is significantly higher than the general population, most remarkable in the population under 35 years of age, this suggests a devastating premature aging process and the effects of the bowel on the kidney-bone axis. Further analysis including the presence of osteopenia in this population is needed to elucidate this finding.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-204 - Risk factors for abnormal imaging after the first febrile urinary tract infection in 0- to 3-month-old infants: a retrospective cohort study

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Objectives: To assess the association of clinical factors and investigation results with imaging abnormalities (ultrasound of the kidneys, ureters and bladder [US KUB], dimercaptosuccinic acid scan [DMSA] and/or micturating cystourethrogram [MCU]) and recurrent urinary tract infections (UTIs) in 0- to 3-month-old infants presenting with their first febrile UTI.
Methods: We conducted a retrospective cohort study of 0- to 3-month-old infants with first febrile UTI admitted from 2010 to 2016. Logistic regression model was used to analyze the associations of imaging abnormalities (US KUB, DMSA and/or MCU) (primary outcome) and recurrent UTI (secondary outcome), with covariates selected *a priori*: age at presentation, maximum temperature, duration of illness at presentation, interval between start of antibiotics and resolution of fever, C-reactive protein (CRP), total white cell count on the complete blood count, bacteremia, white blood cell count on the urinalysis and non-Escherichia coli (non-E coli) growth in the urine culture.
Results: There were 190 patients but 12 did not undergo routine imaging of the kidneys. Median age at presentation was 63 days (IQR 41-78). There were 24 patients who had the primary outcome. Elevated CRP (adjusted odds ratio [aOR] 1.01, 95% confidence interval [CI] 1.00-1.03, p=0.016) and non-E coli UTI (aOR 5.01, 95% CI 1.65-15.24, p=0.004) were independently associated with abnormalities on imaging, while bacteremia (aOR 4.93, 95% CI 1.25-19.43, p=0.022) and non-E coli UTI (aOR 5.06, 95% CI 1.90-13.48, p=0.001) were independently associated with recurrent UTI.
Conclusion: Risk factors such as elevated CRP, non-E coli UTI and bacteremia at the first febrile UTI in 0- to 3-month-old infants may be useful to predict abnormal renal imaging or recurrent UTI which may influence management after treatment of the UTI.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-207 - A 15-year retrospective review of urodynamic studies in children at Red Cross War Memorial Children's Hospital, Cape Town, South Africa

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Background: Urodynamic study (UDS) has been demonstrated to be useful for the accurate diagnosis of lower urinary tract conditions and, presently, has become the gold standard in the diagnostic assessment of children with neurogenic lower urinary tract dysfunction (NLUTD). Despite its undeniable diagnostic benefits, the adoption of UDS into clinical practice in Africa has been slow. This study aimed to review the use of invasive UDS in children at a tertiary paediatric hospital in South Africa.
Methods: A retrospective analysis of 1108 UDS was conducted. Patient demographic characteristics, primary diagnosis, indication and urodynamic outcomes were reviewed. Presence of urodynamic high-risk features were documented, and a comparison was made between the first study and follow-up study.
Results: This study revealed increasing trends in the use of UDS from 2015. Referrals were from Urology (37.7%), Spinal defects clinic (34.4%), Nephrology (20.8%) and other departments (7.0%). The most common reason for referral was review of medical treatment (36.5%). Spinal dysraphism (58.3%) accounted for the majority of conditions seen. Majority (59.1%) of the patients were receiving more than one type of bladder treatment at the time of their first study, with clean intermittent catheterisation (46.5%) being the most common form of bladder management. 97.5% of studies were performed using transurethral bladder catheterization. Urodynamic diagnosis was neurogenic in 74.0%, anatomical (12.2%), functional (8.8%) and normal (5.0%). There was statistically significant improvement in bladder compliance, detrusor leak point pressure and detrusor sphincter dyssynergia between the first study and a subsequent study following therapeutic intervention.
Conclusion: This study has highlighted the additional benefits of UDS over traditional modalities. The unique ability of UDS to demonstrate changes in detrusor pressures, which is a common reason for therapy failure, makes UDS an invaluable tool in the diagnosis and management of children with lower urinary tract dysfunction.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-208 - "Spending a penny, but keeping it clean" - Reducing the rate of contaminated non-invasive urine samples in the paediatric department

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Aims: When investigating for urinary tract infection (UTI), contaminated samples can lead to delays to diagnosis, inappropriate antibiotics and unnecessary follow-up. Reported contamination rates for non-invasive urine samples range from 14.3-26% for clean catch samples[1], and from 12.2-29% when using pad samples[2,3]. We hypothesised that our baseline contamination rate was higher than this, and our aim was to reduce this by 50% from baseline over 6 months.
Methods: Data was collected weekly using a laboratory database search. Primary outcome measure was the number of contaminated non-invasive urine samples per PDSA cycle as a percentage of total non-invasive urine samples. Exclusion criteria: > 16 years; samples requested from other sources; patients with a mixed growth urine culture who were treated as a having a UTI based on positive microscopy or nitrate-positive urinalysis, clinical presentation and clinician decision-making.
Change ideas aimed at reducing the rate of contaminated non-invasive urine samples were introduced

1. Staff & parent focus groups
2. Introduction of an information leaflet
3. Trial of the "Quick-Wee" method[4]
4. Staff education session and use of infographic
5. New method for urine pad use[3]

Results: Baseline contamination rate was 42.8-47%. We demonstrated sustained improvement, achieving our target by PDSA cycle 3. Shift in consecutive data points below the median indicated non-random variation. The contamination rate in subsequent cycles remained below the median, however there is a tendency towards increasing contamination rate.
Conclusion: We used multiple small tests of change and engaged front line users to achieve our goal. Continuous improvement takes time and sustained effort. There are further change cycles planned to optimise the use of urine pad samples when used as second preference, as well as expansion of these improvement methods to the emergency department.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-210 - Giggle Incontinence is rare, troublesome but treatable

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Background: Laughter induced daytime urinary incontinence (DUI) can be seen with both giggle incontinence (GI) and bladder dysfunction (BD). True GI, where DUI occurs exclusively with laughter with otherwise normal bladder function, is rare. In BD, DUI occurs with laughter but also with other activities increasing intraabdominal pressure (coughing, jumping etc.). GI is often confused with BD.
Case Description: An 8-year-old girl with no medical history presented with DUI since age 5 years after achieving toilet-training at age 3 years. Sudden, moderate volume DUI with laughter (but not giggling) occurred weekly; smaller pre-void leakages with a full bladder occurred infrequently. No DUI occurred with coughing, sneezing, or jumping. Patient denied urgency, frequency, dysuria, bedwetting, constipation, or urine infections. Maternal grandmother underwent childhood urethral surgery with unknown details. Physical examination and urine studies were unremarkable. Ultrasound showed normal kidneys and bladder emptying. Laxative and anticholinergic therapy were initiated. Symptoms persisted causing anxiety at school. Anticholinergic dose was increased, and biofeedback (pelvic floor therapy) was added. About 2 months later, patient experienced improvement with less frequent and smaller DUI episodes.
Discussion: Urinary incontinence is stressful for children. GI is a rare cause of DUI starting at age 5-7 years and mostly affects girls. Exact pathogenesis is unclear; a neuro-urologic disorder causing central detrusor instability is suspected. Wetting frequency is variable. Urgency is unusual but may be seen. Therapy is not standardized. Some report GI as a debilitating, difficult to treat condition. Non-pharmacologic interventions (hydration, voiding schedule, biofeedback) and medications (anticholinergic, stimulant) have been used. An initial combined non-pharmacologic and anticholinergic therapy did not help. Addition of biofeedback led to improvement. In conclusion, GI is marked by DUI with laughter but not giggling, urge incontinence may be seen and symptoms are treatable. Awareness of the difference between GI and BD is essential to optimize management.

Urology (including UTIs, kidney stones and bladder dysfunction)
P1-211 - evolution of children and adolescents with lower urinary tract dysfunction

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Objective: To evaluate the clinical and evolution characteristics of patients with lower urinary tract dysfunction(LTUD) and the factors associated with the evolution of these patients.
Methods: A retrospective study of 125 patients with LTUD. The patients with neurogenic bladder, lumbosacral dysrrhaphy, chronic kidney disease and tubulopathies were excluded . The information was obtained from the database.
Results: The mean age was 7.84±2,51y (5 to 15,08y) and 63.2% female. The symptoms were increased urinary frequency in 52.5% (44/84), decreased urinary frequency in 5.9% (5/84), intermittent incontinence in 100%, daytime incontinence in 72.6% (90/124), enurese in 69.4% (86/124), urgency in 37.6% (47/125), weak urine stream in 3.6% (3/118), disuria in 16% (7/125). Urinary tract infection has been reported in 36.3%, constipation in 52.4%, family history of daytime incontinence in 1.1% and family history bedwetting in13.6% of the patients. Early unfurl occurred in 30.8%. Urotherapy and treatment of constipation and vulvovaginitis were performed in all patients. During follow-up 17.6% did not return for medical appointments. Adherence to urotherapy was complete in 39.8% (41/103) and partial in 21.3% (22/103). In patients with daytime incontinence, 51.4% presented disappearance of symptoms. There was no association with constipation and family history. The mean follow-up time was 18 months and the mean time for symptom improvement was 9.19 months. In patients with enuresis, 40.7% presented disappearance of

symptoms. There was no association with constipation and family history. There was an association with a family history of enuresis. The mean follow-up time was 19 months and the mean time for symptom improvement was 13.9 months. Adherence to urotherapy was significantly associated with the disappearance of symptoms in patients with daytime incontinence.
Conclusion: Urotherapy should be reinforced in children with LTUD, clinical improvement occurs in more than 70% of patients, mainly in services that have difficulties with other treatments (physiotherapy, biofeedback).

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-212 - Non pharmacological therapy in children with bedwetting : is it effective ?

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Background & Objective: Enuresis or bedwetting is not so uncommon in children though the prevalence varies according to age. Spontaneous remission may occur on bedwetting at a rate of approximately 15 % per year, but management should be carried out because of its deep impact on a child's emotional state, self-esteem, families, social daily life and global quality of life. Non pharmacological therapy is an appropriate initial therapy for bedwetting in which both the parents and children are motivated to take the behavioral approach. This study aims to determine the effectiveness of non-pharmacological therapy in children with bedwetting.
Method: A prospective observational study was carried out in children of 5 to 15 years with the complaints of bedwetting visited the OPD of Asgar Ali Hospital during January 2021 to December 2021. Bedwetting was categorized in to primary and secondary enuresis; monosymptomatic and non monosymptomatic enuresis group according to the definition of International Children's Continence Society (ICCS). Also children were divided into different age group, Group A-5-7 years, Group B -8-10 years and Group C- >10 years, and the response is divided as no response - <50%, partial response-50-99% and complete response–100% reduction from the baseline symptom frequency.
Result: Among 74 patients, 28 (38%) are male and 46 (62%) are female, majority of them had primary enuresis 72 (97%) only 2 patients had secondary enuresis. Maximum was monosymptomatic 62 (83.7%), non-monosymptomatic were only 12 (16%). Among 32(43%) patients of group A,87.5% had complete response within 3 months of follow up, in group B total 20 (27%) patients, 40% had complete and 40 % had partial response but in group C, among 22 (30%) patients only 9% had complete and 46% had partial response.
Conclusion: Non pharmacological therapy in children with bedwetting showed encouraging recovery.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-213 - Role of bladder diary and imaging for initial assessment of causes of increased daytime frequency in children. - An observational case series.

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Introduction: Several functional and organic disorders of voiding are noted in children presenting as increased day time frequency with urgency .The condition is quite troublesome if associated with incontinence and negatively impacts the mental health of the child. The causes are often difficult to ascertain clinically and may range from pollakiuria to complex causes and parents feel concerned and helpless as repeated urinary samples test negative for infections.
Methods: All children presenting to the out patient department with increased daytime frequency with or without enuresis were evaluated clinically. Routine urinary analyses, voiding bladder and bowel diaries and a renal ultrasound scan were advised. Based on the above findings further investigations like cystourethrogram, urodynamic studies were undertaken if required.
Results: 36 children were evaluated between November 2020 to March 2022.
19 were boys. 10 children had associated nocturnal enuresis. None of the children suffered from hypertension or diabetes. Hypercalciuria was noted in six children from spot urine analysis.
Bladder diary over 48 hours showed increased frequency of more than 15 times per day in all children. 30 had maximum voided volume as per expected bladder capacity, though most urine volumes were much less than expected. Total intake correlated with output in 100% patients. Renal ultrasound scan noted increased post-void residue in 60% children. 70% had increased rectal diameter suggesting constipation.6 children had history of recurrent urinary infections and 4 had structural anomalies. 6 children needed urodynamic study.
Conclusion: Pollakiuria is one of the commonest causes of increased daytime frequency. Bladder diary and ultrasound are most useful in initial assessment of these cases.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-215 - Predicting antidiuretic response to desmopressin in nocturnal enuresis

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Background: Nocturnal enuresis is caused by nocturnal urine production and functional bladder capacity mismatch. ICCS suggests patient classification into MNE and NMNE, where MNE is likely to respond to desmopressin and/or alarm. This led to the misconception that NMNE could not benefit from desmopressin. With the recent ICCS standardization, most patients are now labeled NMNE. Desmopressin's antidiuretic effect and renal concentrating response have no direct correlation with bladder dysfunction and should be evaluated independently. Many patients have LUTS and nocturnal polyuria and could benefit from desmopressin in combination therapy.
Methods: Aim: identify patients in a tertiary center who might benefit from desmopressin (defined as urinary osmolality (Uosmol)<850 mOsm/l) and study the timing overnight.
Methods: retrospective analysis of 398 enuretic children who performed a 24h-urine concentration profile at home (4 daytime (D1-D4), 4 nighttime urine collections (N1-N4)).
Results: 212 children (>50%) had Uosmol<850 mOsm/l at the 1st-night collection (N1), and would benefit from a short-term desmopressin activity; however, in a significant percentage, Uosmol is low later in the night (181 N2, 169 N3, 167 N4), needing a longer action duration.

50 patients didn't reach Uosmol>850mOsm/l over 24h, suggesting lower maximal renal concentration capacity of the normal spectrum or high 24h fluid intake.
Conclusion: Classification into MNE and NMNE is mainly bladder/LUTS driven and is widely accepted to predict the anti-enuretic effect of therapy, thus an indication for desmopressin. However, many patients have a combination of LUTS and abnormal circadian diuresis pattern. Desmopressin's anti-diuretic effect may be expected in most patients with high diuresis and low Uosmol overnight. >50% of patients have a low Uosmol early the night, hence a therapeutic window for desmopressin. In 1/3 patients, Uosmol remains longer low, needing longer-acting V2-stimulation, without risk of too prolonged action. It is evident that desmopressin's PK/PD characteristics do not fulfill these promises.

Urology (including UTIs, kidney stones and bladder dysfunction)

P1-216 - Hyperoxaluria and low calcium intake in pediatrics: beware of diet!

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Introduction: Secondary hyperoxaluria may be due to increased dietary intake of oxalate/oxalate precursors, decreased calcium intake or intestinal malabsorption. In pediatrics, primary genetic forms (PH) are the most frequent, but in adults, almost half cases of hyperoxaluria have a nutritional origin.
Case: We report on a 5-year-old girl, referred to our tertiary care for hyperoxaluria. She was a single child born from non-consanguineous parents without familial renal history. She displayed cloudy urines in infancy; renal ultrasounds found multiple bilateral lithiasis. A first evaluation was performed, finding high levels of urinary oxalate/creatinine ratio (Ox/creatU), between 120-304 µmol/mmol (N 17-100). Genetic analysis ruled out PH 1, 2 and 3.
A thorough evaluation was then performed because of the discrepancy between overt hyperoxaluria and negative genetic testing. The patient also had multiple food allergies (including cow's milk protein). A detailed nutritional assessment found a low-calcium diet, with only 340 mg of nutritional calcium per day (as opposed to the recommended 800 mg for age), only of vegetal origin (thus of lower efficiency for calcium intestinal absorption). She did not receive calcium supplementation. Biochemical evaluation found normal renal function, and confirmed hyperoxaluria (Ox/creatU 132) with normal glycolate, as well as normal calcium, phosphate, PTH and ALP levels but increased 1.25-dihydroxyvitamin D (350 pmol/L, N <200) and hypocalciuria (<0,11 mmol/L).
Dietician advice were given, aiming at normal calcium intake. Six months later, both 1.25-dihydroxyvitamin D and Ox/creatU normalized (86 µmol/mmol and 157 pmol/L, respectively), as well as renal ultrasounds.
Discussion: Enteric hyperoxaluria is common in adults, but less frequent in children. Low calcium intake in children may be seen more frequently, because of increased prevalence of cow's milk allergy, avoidance of dairy products and vegan diets. A thorough dietetic assessment is crucial in the evaluation of pediatric nephrolithiasis.

Ciliopathies (including ARPKD and nephronophthisis)

P2-218 - Clinical Presentation and Outcome of Ciliopathies --- Birth to Teens

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Ciliopathies have common but variable time of occurrence of pathogenesis and a spectrum of underlying genetic variations
This heterogenic pattern is also translated into the clinical presentation of Ciliopathies. Autosomal Recessive Kidney Diseases (ARPKD) and cystic dysplastic syndrome related to the cystic transformation during kidney development while Autosomal Dominant Kidney Diseases (ADPKD) and Juvenile Nephronophthisis (JNN) happening after renal development.
Considering this basic fact ARPKD present in early neonatal life and infancy while ADPKD and JNN have a subtle course and present at around first decade.
We would like to share presentation and outcome of our ciliopathies patients from a tertiary care under resourced region where antenatal diagnosis is not made many times and the limited availability of renal replacement therapies for young infants with ciliopathies leave the physician and parents at a hopeless point.
We managed 19 patients between2019-2021. There were 15(78.9%) male.
14(74%) of ARPKD and 3(16%) of JNN and 2(10.5%) of Infantile Nephronophthisis. Among ARPKD 4(28.5%) had antenatal presentation while 10(71.4%) in the first year of life. 11(79%) patients of ARPKD had the first presentation with Renal failure. 5 patients required acute peritoneal dialysis for acute metabolic and volume control. Ultrasound findings of ARPKD were enlarged echogenic kidneys. Hepatic involvement among ARPKD was found in 5(35.7%). Common hepatic findings were moderate dilation of intrahepatic ducts, increased hepatic echogenicity. Extra renal manifestation were dominant in JNN. Ophthalmological abnormalities were found in all JNN patients followed by Polydactyly. All patients of JNN presented with renal failure and are on long term dialysis awaiting renal transplant. Among the ARPKD 3 expired due to renal failure, 8 alive in follow up in non dialytic stage of CKD.

Ciliopathies (including ARPKD and nephronophthisis)

P2-221 - A child case of nephronophthisis cause by mutation of CEP164 gene

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Objective: To discuss the clinical manifestations and diagnostic experience of nephronophthisis.
Methods: Summarize the clinical data of one child with nephronophthisis who was diagnosed by multidisciplinary consultation in the in the Center for Rare Diseases of Beijing Children's Hospital , Capital Medical University , National Center for Children's Health in December 2021.
Results: The clinical manifestations of this case were transient gross hematuria, persistent microscopic hematuria, progressive renal insufficiency, and cutis marmorata telangiectatica congenital. This patient carries a compound heterozygous mutation in CEP164.Pathological examination of kidney showed thrombotic microangiopathy renal injury combined with intracapillary proliferative glomerulonephritis and tubulointerstitial nephritis. After multidisciplinary consultation, the diagnosis of nephronophthisis was considered after comprehensive consideration of the clinical manifestations, pathological and genetic

results of the child. Further functional verification of genetic testing is planned to clarify the pathogenicity of compound heterozygous mutations in the CEP164 gene.
Conclusions: Nephronophthisis is a rare disease, and the understanding of it should be improved, especially the gene mutation of CEP164.

Ciliopathies (including ARPKD and nephronophthisis)

P2-222 - A Monoallelic IFT140 Pathogenic Variant in a Child with Polycystic Kidney Disease

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Background: There is broad genetic heterogeneity underlying polycystic kidney disease (PKD) in children, including autosomal dominant (ADPKD), recessive polycystic disease (ARPKD), and ciliopathies with more syndromic involvement. Biallelic pathogenic variants to *IFT140,* encoding the cilia-associated protein IFT140, cause short-rib thoracic dysplasia-9 with or without polydactyly (SRTD9), while a mild ADPKD-spectrum phenotype was recently reported in adult monoallelic individuals. We have used broad genetic screening approaches to analyze genetically unresolved childhood PKD.
Design/Methods: Genetic testing in childhood PKD patients was performed at Mayo Clinic PKD Center employing a PKD/ciliopathy gene panel of 357 genes.
Results: We report a pediatric patient with a specific monoallelic large *IFT140* deletion, c.1524+1418_1653-85del10.9kb (p.Gly509fs). She was incidentally found to have cysts in her kidneys at 11 years of age by a computed tomography scan performed to evaluate abdominal pain. Clinical genetic testing was negative for *PKD1, PKD2, PKHD1, and HNF1B.* There was no known family history of PKD, though neither of her parents had kidney imaging studies. During her last follow-up at 15 years, she maintained a normal glomerular filtration rate, blood pressure, and was negative for proteinuria. Magnetic resonance of the abdomen revealed numerous bilateral kidney cortical cysts. The largest cyst, located in the left upper kidney pole, measured 1.2 x 1.7 x 1.7 cm. Her kidneys were above the normal 95th percentile in size for age/height, but small for ADPKD; height adjusted TKV = 290 (mL/m), consistent with the Mayo Clinic Imaging classification of 1A for ADPKD.
Conclusion: Although monoallelic *IFT140* pathogenic variants are associated with a mild adult ADPKD phenotype, finding an *IFT140* deletion in a pediatric patient with multiple, bilateral cysts indicates that this gene should be considered when screening childhood PKD patients with a negative or positive family history.

Ciliopathies (including ARPKD and nephronophthisis)

P2-225 - Anemia and progression to end-stage kidney disease among children with nephronophthisis

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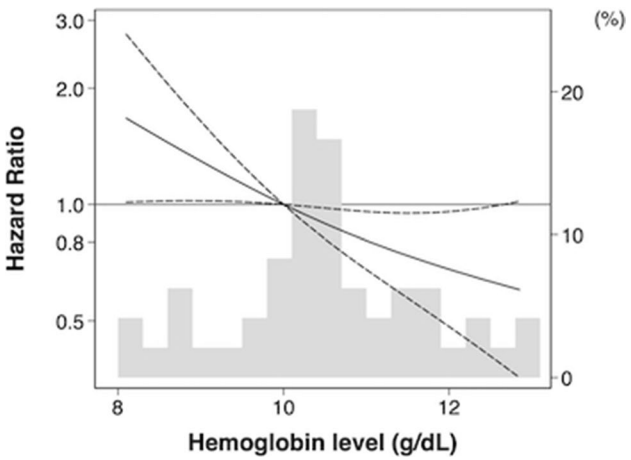
Background: Anemia is one of the common complications of chronic kidney disease (CKD), and is associated with various adverse consequences. However, data are scant on the association between anemia and progression to end-stage kidney disease (ESKD) among children with pre-dialysis CKD due to nephronophthisis. Epidemiological information on nephronophthisis is also insufficient.
Methods: We estimated the incidence and prevalence rates in Japan based on a national database consisting of 90 children with nephronophthisis. In a cohort study of pre-dialysis children, we examined the association of hemoglobin levels with risk for progression to ESKD, defined as receiving renal replacement therapy, using a Cox proportional hazards regression adjusted for age, sex, extrarenal manifestations, hypertension and estimated glomerular filtration rate.
Results: The estimated incidence/prevalence rates of nephronophthisis were 0.32/3.4 per million age-related population. The analytical cohort included 62 children with available baseline hemoglobin data. Among them, median age at the first hospital visit was 9.0 (interquartile range: 6.1–12.1) years and mean ± SD baseline hemoglobin level was 10.7 ± 2.9 g/dL. Forty-seven children progressed to ESKD during the follow-up period. A crude rate of ESKD progression was 0.26 per patient-year. There appeared to be a trend toward higher risk for progression to ESKD across lower hemoglobin level. The hazard ratios (95%CI) for progression to ESKD were 1.67 (1.01–2.76), 1.37 (1.02 to 1.83), 0.81 (0.68–0.96), and 0.69 (0.5 to 0.95) at hemoglobin levels 8.0, 9.0, 11.0, and 12.0 g/dL, respectively (reference: 10.0 g/dL) [Figure].



Conclusions: The incidence and the prevalence of nephronophthisis in Japan might be lower than other countries. Anemia was associated with high risk for progression to ESKD among children with nephronophthisis.

Ciliopathies (including ARPKD and nephronophthisis)

P2-226 - Height trajectory during the pretransplant period in children with nephronophthisis

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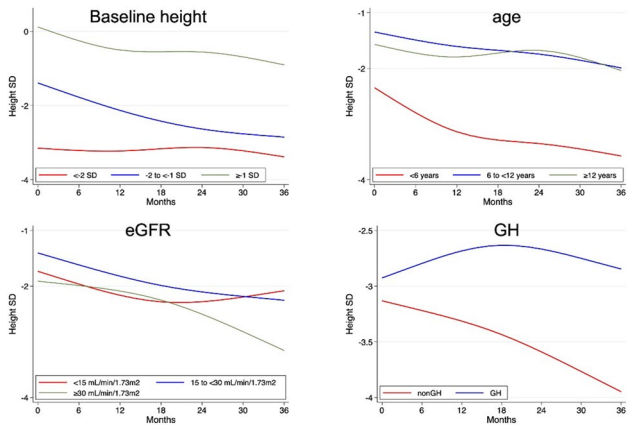
Background: Although height gain is one of the main goals in the management of nephronophthisis in children, height trajectory before kidney transplantation is not well described.
Methods: In a national cohort of 73 predialysis and dialysis patients with nephronophthisis aged ≤18 years between 1997 and 2018, we estimated the 3-year height trajectory until kidney transplantation using linear mixed-effects models stratified by baseline height SD score, age, estimated glomerular filtration rate (eGFR) and growth hormone (GH) therapy. In GH analysis, we restricted the cohort consisting of 45 patients who experienced short stature (height <-2 SD).
Results: Median age at the first hospital visit was 9.0 (interquartile range: 5.7–12.1) years and mean baseline height SD score was -1.7 ±1.7. Among 45 patients with short stature, 20 (44%) received GH therapy. As a whole, a decreasing trend in height SD score was observed. Baseline height <-2SD had a stable trajectory compared with ≥-2SD. Younger age <6 years showed a steeper decline in height SDS score than ≥6 years old. eGFR <15 mL/min/1.73m^2 was associated with mild decline compared with ≥15 mL/min/1.73m^2. Patients receiving GH therapy gained height compared with those who did not [Figure]. After excluding 4 patients with skeletal complications (1 Jeune syndrome, and 3 Sensenbrenner syndrome) as sensitivity analyses, consistent results were observed.



Conclusions: Height gain is poor during the pretransplant period in nephronophthisis. However, baseline height <-2SD and eGFR <15 mL/min/1.73m^2 may be associated with milder height loss. GH therapy may contribute to height gain.

Ciliopathies (including ARPKD and nephronophthisis)

P2-228 - Long-term clinical features of mild case with autosomal recessive polycystic kidney disease (ARPKD) diagnosed by genetic analysis

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Previously most cases of autosomal recessive polycystic kidney disease (ARPKD) are thought to have severe symptoms in the neonatal period with renal dysfunction. But recent advances in genetic analyses have made it possible to diagnose mild cases with ARPKD. Therefore, it is presumed that there are a considerable number of undiagnosed mild cases with ARPKD.
Patient: The case is a 16-year-old woman. A small renal cyst was pointed out by fetal echo and was introduced to our hospital at the age of 1 month. She had no family history of cystic kidney disease and has regularly performed blood tests and image evaluations of renal cysts. Genetic analysis performed at the age of 6 identified two presumed pathological variants of the *PKHD1* gene (c.7091T> A, c.9629C> G) and diagnosed as ARPKD.
Objectives of the study: To clarify the long-term disease course of the patient with mild ARPKD.
Methods: We show the progress of renal and liver functions, and MRI images of renal cysts over 16 years. In addition, the correlations between the *PKHD1* gene variants and clinical phenotypes have also been investigated.
Results: At present, there are gradual enlargement and increase of renal cysts, but the renal function is normal. And no hypertension and liver signs were observed at the latest observation.
Conclusion: In ARPKD, it is important to observe carefully and share mild and moderate cases, considering the awareness and dissemination of the disease concept and future drug treatment targets.

Ciliopathies (including ARPKD and nephronophthisis)

P2-232 - Clinical polymorphism Barakat syndrome

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Barakat Syndrome (MIM#146255) is a rare autosomal dominant disease caused by GATA3 gene mutation and manifested by hypoparathyroidism (H), sensorineural deafness (D), and renal disease (R). HDR syndrome characterized by high clinical variability and prognosis.
We present two patients with different phenotypes of Barakat Syndrome.
Patient 1st is a 12 old boy with antenatally diagnosed cystic kidney dysplasia, congenital deafness and hypoparathyroidism manifested at age of 1 year (hypocalcemia, hypomagnemia, hyperphosphatemia). He developed CKD at age of 12 years, his eGFR is 67 mL/min/1.73m2
Patient 2nd is a 7-years old boy with cystic kidney dysplasia (revealed antenatally) and bilateral vesico-ureteral reflux grade III (diagnosed at age of 1 year) and kidney scars development (DMSA -scan). An increase in blood creatinine level has been noted since birth, and now his eGFR is 25,5 mL/min/1.73m2. The boy also had congenital deafness, but hyperparathyroidism with normal calcium blood level during all time of observation.

De novo heterozygous mutation in the gene GATA3 was detected in both patients.
Our observations demonstrate an antenatal presentation of GATA3-related cystic kidney diseases, variability of clinical phenotypes and different kidney prognosis of patients with Barakat Syndrome. The syndrome should be suspected in cases of early high-grade deafness and kidney disease presentation for the purpose of early diagnosis and appropriate therapy including the prevention of CKD progression.

Ciliopathies (including ARPKD and nephronophthisis)

P2-233 - Screening for treatable manifestations of ADPKD diagnosed in childhood - a multicentre study

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Introduction: Children with ADPKD are identified incidentally following abdominal ultrasound or due to parental choice for screening in affected families. Once identified, regular measurement of blood pressure and proteinuria, treatable manifestations of ADPKD are recommended.
Aim of the study: To assess the prevalence of treatable manifestations of kidney involvement in an unselected cohort of children/adolescents with ADPKD.
Material and methods: A multicentre, cross sectional study of 227 ADPKD children/adolescents identified at ten pediatric nephrology centres was performed. Initial diagnosis was made in 30% before 5yrs, in 24%, 29%, 18% between 5-10, 10-15, >15yrs of age respectively. Kidney involvement was assessed at a mean age of 12.8 yrs (0.24-20.8yrs) by ultrasound, hypertension (HP) by office BP measurements and ABPM, albuminuria by laboratory assessment of morning urine samples, eGFR by modified Schwartz formula.
Results: Kidney ultrasound demonstrated at least 3 kidney cysts >1cm in size in 137/206 (66.5%) children, including 69 children (33.5%) with ≥10 visible kidney cysts. Hypertension, diagnosed by office BP measurements, was present in 32.7% (67/205) of subjects; 25.8% (53/205) of measured systolic values and 14.1% (29/205) of diastolic values exceeded the 95th centile. Elevated (≥95 centile) values of 24hr mean arterial pressure (MAP) was found in 13.9% (12/86), 24 hr SBP in 18.6% (19/102) and 24hr DBP in 10.8% (11/102) of tested subjects. Night SBP and DBP exceeded 95th centile in 24.5% and 17.6% of children. Albuminuria >20mg/l was present in 33.3% (27/81) and eGFR <90ml/min/1,73m^2 in 20.3% (27/133) of the studied subjects. Thirty one percent (71/277) of the cohort received antihypertensive treatment.
Conclusions: 1. A large proportion of paediatric subjects with a positive family history fulfil adult imaging criteria for the diagnosis of ADPKD.
2. Childhood ADPKD is not universally asymptomatic as a significant proportion of children demonstrate hypertension, albuminuria or decreased eGFR which require management.

Ciliopathies (including ARPKD and nephronophthisis)

P2-234 - Lack of fibrocystin results in progressive kidney and liver disease associated with pathogenic STAT3 activation in murine Pkhd1-knockout

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[3]*University of Zurich, Institute of Anatomy and Zurich Center for Integrative Human Physiology ZIHP, Zurich, Switzerland*

Objectives: Loss of fibrocystin function causes autosomal recessive polycystic kidney disease (ARPKD) associated with epithelial defects, cyst formation and fibrosis of kidney and liver. Variable outcome of the disease in children is attributed to the type of mutation of both alleles of the *PKHD1* gene and genetic background. So far, study of fibrocystin function in mouse kidney was hampered by mild cyst development and late onset in available *Pkhd1*-knockout animals. Here, we re-analyze the kidney phenotype in female *Pkhd1*-knockout mice of different age in a defined background strain and observe consistent characteristics and hallmarks of disease development.
Methods: Targeted mutation *Pkhd1*-knockout mice in BALB background were maintained within the line, and kidneys of females, homozygous and heterozygous for the *Pkhd1*-knockout allele as well as wildtype, analyzed histologically at 3, 6 and 9 months of age with serum and urine samples taken before preparation. We compare epithelial defects to induced renal epithelial cells (iRECs) with *Pkhd1*-knockout and re-expressors derived from the very mouse line.
Results: At 6 and 9 months of age, relative kidney and liver weights were massively increased in homozygous *Pkhd1*-knockout mice as compared to heterozygous and wildtype controls. In kidney, cyst formation at the corticomedullary border led to a significantly increased cystic index in knockout mice associated with pronounced macrophage recruitment and fibrosis peaking at 9 months. In addition, proliferation markers were significantly enhanced and nuclear localization of phosphorylated STAT3 was observed in cyst lining epithelia. Induction of STAT3-dependent signaling was addressed in cystic mouse tissue and in stimulated *Pkhd1*-knockout and fibrocystin re-expressing iRECs.
Conclusions: Maintenance in defined BALB background leads to a murine *Pkhd1*-knockout model showing progressive renal cyst formation with fibrosis and activation of STAT3 signaling, allowing analysis of disease related mechanisms and testing of therapeutic interventions.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-235 - Variability in response to iron sulfate therapy in children with chronic kidney disease and anemia

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Anemia is a common complication of CKD in children and oral iron, usually ferrous sulfate, is recommended as the initial therapy. However, response to iron therapy in children with pre-dialysis CKD remains poorly investigated.
We reviewed medical records of children with CKD stages I-IV from two New York metropolitan area medical centers (2010 to 2020) who met KDIGO definition of anemia and were treated with iron sulfate. Response to therapy was assessed by improvement of anemia, resolution of anemia using KDIGO definition, and changes in iron status (the latter was also used as a measure of compliance). Potential predictors and correlates of treatment response were assessed using univariate and multivariate (adjusted for age, sex, and GFR) regression analyses. Study criteria were met by 65 children (35 males) with average time between visits 102 days. The average GFR was 52.1 mL/min/1.73m^2, and 40.7% had glomerular CKD. Following iron therapy, hemoglobin improved from 10.2 to 10.8 g/dL ($p<0.001$), hematocrit from 31.3 to 32.8% ($p<0.001$), serum iron from 49 to 66 mcg/dL ($p<0.001$), transferrin saturation from 16 to 21.4% ($p<0.001$). There was an insignificant decrease of serum ferritin (55.0 to 44.9 ng/mL). Anemia has resolved in 29.3% of children. No improvement in hemoglobin/hematocrit was seen in 35% of children, and no transferrin saturation improvement in 26.9%. There was no correlation between changes in hemoglobin and changes in transferrin saturation/serum iron. A negative correlation between changes in hemoglobin and changes in ferritin ($r=-0.37$, $p=0.03$) was observed. Children with more severe anemia and lower alkaline phosphatase at baseline had better response to iron therapy ($p<0.001$).
Thus, anemia was resistant to the initial course of iron sulfate therapy in approximately 30% of children with CKD in this cohort. Resistance did not appear to be related to non-compliance or disease severity but could be related to CKD-mineral and bone disorder.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-236 - Serum GDF-15 as a novel biomarker of CKD progression in children

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[4]*on behalf of the ESCAPE and 4C Research Consortium, Heidelberg University Hospital, Heidelberg, Germany*

Introduction: There currently is limited ability to diagnose and predict the progression of chronic kidney disease (CKD) in children using biomarkers. Growth differentiation factor-15 (GDF-15) has been identified as a promising biomarker of the proceeding of CKD in adults. High serum levels are associated with an increased risk of CKD progression. We investigated the association of serum GDF-15 levels with CKD progression in children, using large European CKD cohorts. We additionally considered urinary epidermal growth factor (uEGF), a recently identified independent biomarker of pediatric CKD progression.
Methods: We performed a post hoc analysis of the *Cardiovascular Comorbidity in Children with CKD* (4C) study, which prospectively followed children aged 6–17 years with baseline estimated glomerular filtration rate (eGFR) of 10–60 ml/min/1.73 m^2. GDF-15 levels were measured in archived serum samples collected from 671 patients within 6 months of enrollment.
The composite endpoint of CKD progression included the start of kidney replacement therapy, 50% eGFR loss, or eGFR <10 ml/min/1.73m^2.
Results: In a Cox proportional hazards model, higher GDF-15 levels were associated with an increased risk of CKD progression (HR 1.66; 95% CI 1.20–2.11) independent of age, sex, baseline eGFR, proteinuria, and systolic blood pressure. Adding GDF-15 and uEGF individually to a model containing these variables significantly improved the C-statistics, indicating improved prediction of the risk of CKD progression. The addition of both markers together improved the C-statistic even further, demonstrating the advantage of combining GDF-15 and uEGF to improve the prediction of CKD progression in children.
These results were externally validated in 222 children of the *ESCAPE trial* cohort, confirming the independent improvement of predictive models by GDF-15 and uEGF.
Conclusion: Serum GDF-15 and urine EGF levels provide complementary information on the risk of CKD progression in children and might be included in future prognostic biomarker panels aimed at personalized, risk-stratified management of pediatric CKD.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-237 - Ophthalmological changes in children with advanced stage of chronic kidney disease- a hospital-based study

Afroza Begum MD- FCPS[1], Amit Datta[1], Ranjit R Roy[1], Golam Muin Uddin[1], syed saimul Huque[1], Tahmina Jesmin[1], Abdullah Al Mamun[1]
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Background: Advanced stage of CKD may cause ocular disorders for many reasons and ocular complications due to disease process cause significant loss of vision.
Objective: To find out the ophthalmological changes in children with advanced stages of CKD and compare the findings among the different stages
Methodology: This cross-sectional study was carried out in department of Pediatric Nephrology, department of Ophthalmology, in a tertiary care hospital from January 2020 to July 2021.CKD was categorized into stage III to stage V (D) according to glomerular filtration rate (eGFR) by using revised Schwartz formula. CKD patients aged 5-18 years who fulfilled the inclusion criteria were enrolled and children with previous eye abnormalities were excluded. All patients underwent

a detailed ophthalmological examination, which was done by same experienced ophthalmologist.
Results: Among 92 patients male: female ratio in CKD was 1.97 (61):1(31) and mean age 12.1±3.68 years. Twenty-nine patients had impaired visual acuity. Decreased visual acuity was observed in left eye and right eye was 59.8% and 54.34% respectively. Lid edema was present in 20.7% patients (p<0.001). Conjunctival pallor was found in 56 patients (60.9% of total eyes). In CKD stage V(D) group nine patients (9.8% of total eyes) were diagnosed as dry eyes (p=0.003). Seven patients (7.6%) had conjunctival congestion. Significantly higher level of serum phosphate, calcium × phosphate was found in the patient having conjunctival congestion and hypertensive retinopathy. Mean intra ocular pressure was in normal range. Fifteen patients (16.3% percent of total patients) had hypertensive retinopathy; significantly in hemodialysis group. Scatter diagram showed left visual acuity had weak positive significant correlation with serum phosphate (r=+.312, p=0.002) and calcium x phosphate (r= +.222, p=0.033).
Conclusion: Hypertensive retinopathy was significantly higher in CKD stage VD andhigher calcium × phosphate was found in the patient having conjunctival congestion and hypertensive retinopathy.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-238 - The use of cinacalcet in dialysis infants: data from a European survey

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Introduction: Secondary hyperparathyroidism (SHPT) is commonly seen in children with chronic kidney disease (CKD) and substantially contributes to morbi-mortality. Cinacalcet has been licensed for children on dialysis above 3 years. Safety and efficacy of cinacalcet in children below 3 years is unknown.
Methods: We performed an ESPN and ERKNet survey on the use of cinacalcet in children below 3 years of age from 2011 to 2021. Eight centers treated patients below 3 years of age, and provided 3 monthly retrospective chart analyses of 26 children. Data are median and interquartile range.
Results: At a median age of 19(13–27) months, 26 patients (CAKUT n=11, ARPKD 5, congenital nephrotic syndrome 3, others 7) received cinacalcet for SHPT and hypercalcemia. At start of cinacalcet serum PTH was 792(411–1397) ng/L, corresponding to 12(6-20) times the upper limit of normal (ULN), calcium 2.56(2.43–2.75) mmol/L, phosphate 1.5(1.2-1.7) mmol/L, phosphate z-score -1.7(-3.2-0.6). Total ALP was 660(492-905) IU/L, and 25-D 69(50-89) nmol/L. Initial cinacalcet dose was 0.4(0.2–0.8) mg/kg/day, maximal dose during the follow-up period of 1.4(0.9–1.8) years was 1.0(0.5–1.2) mg/kg/day. PTH decreased significantly within 9 months (p=0.008), to 62(32–227) ng/L (1.8 (0.4-3.3)-fold the ULN at the last follow-up (p<0.0001). Median serum calcium, phosphate, ALP and 25-D remained stable, but eight infants developed 11 hypocalcemic episodes <2.1mmol/L, of which 6 infants had 9 episodes of hypocalcemia below 2.0 mmol/l. One child suffered from a hypocalcemia-related convulsion, due to non-adherence to calcium substitution. Cinacalcet was discontinued in 3 of the eight children. Precocious puberty was reported in two children.
Conclusion: Cinacalcet given at relatively high doses allows for efficient control of SHPT in children on dialysis below 3 years of age. Meticulous control of serum calcium and calcium balance is mandatory in rapidly growing infants, possible endocrine changes should be considered.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-239 - Long-term glomerular dysfunction in childhood cancer survivors; DCCSS-LATER 2 Renal study

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Background: Nephrotoxicity due to intensive oncological treatment may occur later in life of childhood cancer survivors (CCS). However, long-term follow-up studies are limited. This study aimed to evaluate glomerular dysfunction among very long-term CCS in comparison with matched controls from the general population.
Mehods: In the Dutch Childhood Cancer Survivor Study (DCCSS)-LATER 2 renal study, a nationwide cross-sectional cohort study, 1024 CCS ≥5 years after diagnosis, aged ≥18 years at study, treated between 1963-2001 with nephrectomy, abdominal radiotherapy, total body

irradiation (TBI), cisplatin, carboplatin, ifosfamide, high-dose cyclophosphamide or hematopoietic stem cell transplantation participated. In addition, 500 age- and sex matched controls from Lifelines participated, a prospective population-based cohort study in the Netherlands. The glomerular filtration rate (GFR) was estimated with the CKD-EPI 2012 equation including creatinine and cystatin C. Albuminuria was defined as an albumin-to-creatinine ratio >3 mg/mmol.
Results: At a median age of 32.0 years (interquartile range 26.6-37.4), the GFR was <60 ml/min/1.73m^2 in 3.7% of CCS and 0% of controls. Ten (1.1%) CCS had end-stage renal failure. Chronic kidney disease (CKD) according to age-thresholds (i.e. GFR respectively <75 for age <40 years, <60 for 40-65 years, and <40 for >65 years) was 6.6% in survivors vs. 0.2% in controls. Albuminuria was found in 16.2% of CCS and 0.2% of controls. Risk factors for CKD based on multivariable analyses were nephrectomy (odds ratio (OR) 3.7, 95%CI 2.1-6.4), abdominal radiotherapy (OR 1.8, 95%CI 1.1-2.9), ifosfamide (OR 2.9, 95%CI 1.9-4.4), cisplatin >500 mg/m^2 (OR 7.2, 95%CI 3.4-15.2). For albuminuria, risk factors were TBI (OR 2.3, 95%CI 1.2-4.4), abdominal radiotherapy >30 Gy (OR 2.6, 95%CI 1.4-5.0) and ifosfamide (OR 1.6, 95%CI 1.0-2.4). Hypertension and follow-up ≥30 years were associated with glomerular dysfunction.
Conclusion: Lifetime monitoring of glomerular function in CCS exposed to the identified risk factors based on this study is warranted.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-240 - Chronic kidney disease in children in Algeria

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Background: chronic kidney disease is a serious public health problem, it considerably alters the quality of life of affected children. Current epidemiological data remain insufficient despite all the interest of this pathology.
Méthods: A descriptive retrospective study of 170 children followed in nephropediatrics consultation, for chronic renal failure stage 3,4 and 5, over a period of 5 years, from 2017 to 2022. The inclusion criteria were age below 18 years and a clearnce (shwartz) below 30ml/min/1.73m3
Résults: 170 cases were collected; more than half were in terminal stage of kidney disease. Third of our patient's age was less than 5 years old, with an average age of 6 years. The sex ratio was 1.5. Inbreeding was present in more than 30% of cases. The main reason of consultation was short stature and anemia. The most found etiologies were CAKUT and hereditary tubulo interstitial damage and vesico-ureteral reflux wich was the dominant found uropathy. Extrarenal purification was performed in more than 30% of patients, peritoneal dialysis was the preferred mode in our country, more than 60% of dialysis patients were in CAPD mode. Kidney transplantation was performed in only 4% of cases. Mortality is around 10%, most often of cardiovascular origin.
Conclusion: chronic kidney disease es a real challenge, inventory is an important step to define needs in countries where the speciality of pediatric nephrology should be developed, because of the increased number of new cases. Peritoneal dialysis had improved the life expectancy even for the small wight patients.hight mortality rate is caused by insufficient practice of kidney transplantation in our country.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-241 - Experience of parathyroidectomy in children with Chronic Kidney Disease Metabolic Bone Disease (CKD-MBD) on long standing dialysis

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Background: Children with CKD-MBD develop significant complications. Growth failure and bone deformity are unique among children in addition to bone pain and fractures that occur in adults. Treatment includes controlling hyperphosphatemia, dietary modification, pharmacological agents, and surgery.
Results: We describe 5 patients with end stage kidney disease who have secondary hyperparathyroidism and underwent parathyroidectomy in our center from 2016 to 2022.
Median age during surgery is 10.2 (IQR 8.0-13.0) years with dialysis duration of 5 (IQR4.0-6.5) years. All of them have renal dystrophy and 3 of them were wheelchair bound. Four patients were on peritoneal dialysis with dialysate calcium content of 1.25mmol/L and one on Haemodialysis. Preoperative serum level of calcium was 2.4 (IQR 2.1-2.4)mmol/L, phosphate1.8 (IQR 1.1-1.9)mmol/L, alkaline phosphatase 1524 (IQR 1230-2135)IU/L, and intact parathyroid hormone 145.0 (IQR 56.9-233.5)pmol/L respectively. Despite all patients receiving phosphate binders, Vitamin D analogs and calcimimetics, secondary hyperparathyroidism progressed.
Four patients underwent total parathyroidectomy of which two underwent simultaneous auto transplant. One patient had 3 parathyroid glands removed as the fourth gland was not found. There was no vocal cord damage or bleeding postoperatively. All patients required intravenous calcium infusion for 5 (IQR 3.5-6.0)days and duration of hospital stay is 13 (IQR 8-14)days.
At 3 months post parathyroidectomy, the serum level of calcium was 2.3 (IQR 2.1-2.4)mmol/L, phosphate1.0 (0.7-1.5)mmol/L, ALP level 505 (IQR 400-1050). PTH markedly reduced to 0.7 (IQR0.4-1.2) mmol/L. One patient developed hypocalcemia seizure at 5 months post parathyroidectomy due to non-adherence to calcium and vitamin D supplements. For 3 patients that followed up for one year, there was significant improvement in median height with z score from -3.9 to -3.3 in three patients. They are not wheelchair bound anymore.
Conclusion: Parathyroidectomy is a safe procedure in children with secondary hyperparathyroidism which is refractory to medical therapy. It results in increased growth and improvement of bony deformity.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-243 - Hypothyroidism in children in chronic kidney disease

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Introduction: Hypothyroidism is the state of low level of thyroid hormones in circulation, leads to inadequate neurologic, metabolic effects at target organ. In overt hypothyroidism, according to age-wise cut-off, there is low serum free T4 (FT4), raised thyroid stimulating hormone (TSH) levels. In subclinical hypothyroidism (SCH) there is elevated serum TSH level with normal FT4. Prevalence of SCH is reported around 2% in children. In children epidemiological studies on hypothyroidism especially in chronic diseases like chronic kidney disease (CKD) is scarce.
Objective: To determine the prevalence of hypothyroid cases (overt and subclinical) and to analyse their clinical and biochemical parameters in chronic kidney disease patients in pediatric age group.

Methodology: Single center cross-sectional study conducted at Pediatric Nephrology Division in Kalawati Saran Children's Hospital, New Delhi, India. Data of the patients (Age 1year to 18years) visited in pre-transplant clinic from January 2020 - January 2022, were collected and reviewed. Diagnosed cases of CKD (all stages) were included. Their demographic details, clinical data, baseline laboratory investigations were recorded. All patients' thyroid functions were evaluated by electrochemiluminescence method and Anti-TPO antibody level was sent. SPSS version 23.0 was used for analysis.
Results: Convenient sample size was 35. The baseline clinical and laboratory parameters were depicted in table-1.

VARIABLE	N=35
BASELINE CHARACTERISTICS	
AGE (in months)(mean ± SD)	112.08 ± 50.817
GENDER: Male, n %	26 (74.3%)
Female, n %	9 (25.7%)
Height, mean ± SD (cm)	117.45 ± 25.101
Weight, mean ± SD (kg)	22.145 ± 10.690
Body Mass Index (BMI), mean ± SD (Kg/m^2)	15.168 ± 3.109
Systolic Blood Pressure (SBP), mean ± SD (mm Hg)	98.171 ± 12.64
Diastolic Blood Pressure (DBP), mean ± SD (mm Hg)	62.685 ± 9.190
Blood pressure (BP) staging: Normotensive, n %	27, 77.1%
Elevated BP, n %	2, 5.7%
Stage 1, n %	4, 11.4%
Stage 2, n %	2, 5.7%
eGFR, mean ± SD (ml/min/1.73m^2)	25.156 ± 18.984
CKD stage: 1, n %	0
2, n %	2, 5.7%
3, n%	8, 22.9%
4, n %	13, 37.1%
5, n %	12, 34.3%
TSH, mean ± SD (µU/ml)	4.616 ± 4.958
FT3, mean ± SD (pg/dl)	3.189 ± 1.349
FT4, mean ± SD (ng/dl)	1.77 ± 1.730
Hypothyroids: Subclinical: n %	6, 17.1%
Overt: n %	3, 8.6%
TSH of Subclinical hypothyroids (SCH) mean ± SD (µU/ml)	11.876 ± 8.657
FT3 of SCH, mean ± SD (pg/dl)	3.801 ± 1.502
FT4 of SCH, mean ± SD (ng/dl)	2.264 ± 1.605
TSH of overt hypothyroids, mean ± SD (µU/ml)	38.32 ± 53.418
FT3 of overt hypothyroids, mean ± SD (pg/dl)	2.330 ± 1.949
FT4 of overt hypothyroids, mean ± SD (ng/dl)	0.846 ± 0.128
OTHER LABORATORY PARAMETERS	
Hb g/dl, mean ± SD (g/dl)	9.334 ± 2.024
Blood urea, mean ± SD (mg/dl)	114.48 ± 82.756
Serum creatinine, mean ± SD (mg/dl)	3.6123 ± 3.7416
Serum sodium, mean ± SD (mmol/lt)	139.745 ± 5.67
Serum potassium, mean ± SD (mmol/lt)	4.60 ± 0.758
Serum calcium (total), mean ± SD (mg/dl)	8.997 ± 1.324
Serum phosphorus, mean ± SD (mg/dl)	5.483 ± 1.683
Serum Alkalinephosphatase (ALP), mean ± SD (U/lt)	345.371 ± 376.913
PTH (Parathyroid hormone), mean ± SD (pg/ml)	264.705 ± 252.155
25 HydroxyVitamin D, mean ± SD (ng/ml)	29.405 ± 20.409
Serum Bicarbonate, mean ± SD	20.08 ± 4.289
Spot urine protein creatinine ratio (UP:UC), mean ± SD	2.746 ± 2.324
UP:UC: <0.2, n %	4, 11.4%
>0.2 to 2, n %	13, 37.1%
>2, n %	18, 51,4%

Overall 17.1% cases had SCH, 8.6% cases had overt hypothyroidism. Maximum SCH cases were found in CKD stage 4, and overt hypothyroid cases were found in same frequency in CKD stage 3, 4 and 5. Maximum hypothyroid cases were found when spot urine protein creatinine ratio was >2mg/mg. All cases had antiTPO antibody negative.
Conclusion: The exact correlation of hypothyroidism in children with CKD is yet to be established. Our study revealed significant proportion of hypothyroid cases (both subclinical and overt) in advanced CKD stages and with high proteinuria. Studies with large sample size are necessary for confirmation.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-244 - Social Determinants of Health and Longitudinal Medical Appointment Adherence in Adolescents and Young Adults with Pediatric-onset Chronic Conditions

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Background: Medical appointment adherence (MAA) is associated with better patient outcomes. Longitudinal studies on adolescents/young adults (AYAs) with various pediatric-onset chronic conditions are scant.
Methods: We evaluated MAA in AYA over 11 years as: attended, cancelled, or no show to single or multiple same-day appointments in a longitudinal cohort study and correlated MAA to social determinants of health by estimating multinomial logit models that controlled for patient, disease, and appointment characteristics. This IRB-approved study was conducted at the University of North Carolina Hospitals[GDB1] .
Results: AYAs' characteristics: 14.4±5.5 years old, 48% female; 37% Caucasian; 47% African American; 12% Latino; private insurance 45%; Medicaid only 34%; Medicaid/Medicare 7%; self-pay 7% and Tricare/military 4%. The 375 AYAs had 42,682 appointments over 30,985 patient-days. Mean time between appointments was 31 ± 45 days. MAA rates of attendance, cancellation, and no show were 67%, 21%, and 12%, respectively.
Statistically significant findings on multinomial logit regression models revealed that no-show rates (relative to attendance) were 7.8 and 5.0 percentage points (ppts) higher among African Americans than Caucasians[GDB2] [MOU3], depending on per-day appointment concentration. On multi-appointment days, Latinos were 5.2 ppts more likely than Caucasians to no-show vs. attend. Females were 2.8 ppts more likely to cancel an appointment, with older males (females) more (less) likely to not show up on multi-appointment days. Medicaid-covered (self-pay) AYAs were 4.2 (7.1) ppts more likely to no-show to singleton appointments than those with private insurance. However, there were no statistical differences by insurance status when multiple appointments were scheduled on the same day.
Conclusions: Medical appointment adherence over time is correlated with several social determinants of health.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-245 - The risk of developing chronic kidney disease (CKD) in children who have had acute pyelonephritis, who previously had the coronavirus disease 2019 (COVID-19)

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Introduction: The SARS-CoV-2 virus is characterized by a specific three-dimensional protein structure that has a strong affinity for angiotensin converting enzyme 2 (ACE-2) receptors. X. Zhou et al. (2020) showed that in the urothelium of the bladder, ACE-2-positive cells make up 2.4%, and in the proximal convoluted tubules 4%.
The aim of the study was to determine the laboratory features of the course of AP in children infected with COVID-19 12-18 weeks after the onset of the disease.
Material and methods: The main group consists of 15 patients with AP who had COVID-19, in the asymptomatic or mild form and had elevated IgG to SARS-CoV-2. The comparison group includes 18 patients with AP who have not been infected with COVID-19 (IgM and IgG to SARS-CoV-2 were normal in all children). 12-18 weeks after the onset of AP, laboratory parameters such as erythrocyturia, proteinuria and albumin/Cr coefficients were evaluated in the observed groups of children.
Results: In patients who had previously undergone COVID-19, proteinuria, increased albumin/creatinine ratio and hematuria were more often detected 12-18 weeks after the onset of AP than in the comparison group. When evaluating laboratory parameters 12-18 weeks after the AP debut in the observed groups of children, it was found that 40% of patients in the main group retained urinary syndrome, versus 6% of cases in the comparison group.
Conclusions: Thus, the patients of the main group, in contrast to the comparison group, had a 6 times higher risk of developing CKD.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-246 - Genetic test in the diagnosis of chronic kidney disease.

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Introduction: The overall diagnostic yield of massively parallel sequencing (MPS)-based tests in patients with chronic kidney disease (CKD) is around 30% for pediatric cases. The universal use and lower cost of these techniques makes it possible to reassess patients and, in many cases, achieve accurate diagnoses.
Material and methods: We analyzed all patients with CKD from January 2020 to January 2022. We included patients with available genetic study and those who genetic study was performed because of CKD of unknown etiology or with diseases associated with alterations in the development of the urinary system.
Results: We have included 45 patients mean aged 7,6 (0-17,5 y-old) with CKD under conservative management from our active database. We carried out genetics study in 24 patients. The genetic study was normal in 7 patients (29,1%). We found mutation in 15 patients (62,5 %): hereditary dominant tubulointerstitial nephritis in 5 (one of them mutation in SEC61A1 and four mutations in HNF1B), two patients had Wolf-Hirschhorn's syndrome, one Down's syndrome, one Dent's syndrome, one EYA1's mutation, one Prader-Willi's syndrome, one chromosopathy 10q-/12p+, one deletion 1q21.1q21.2, one two mutation, COL4A1 and POMGNT1, and in one patient dominant polycystic disease. The genetic study was of uncertain significance in two patients (8,3 %).
In the family study, the patient with a 1q21.1q21.2 deletion has an affected sister in CKD on hemodialysis was diagnosed with the same deletion. Another patient with mutation in EYA1, her asymptomatic mother was diagnosed with the same mutation.
Conclusions: In our series, the percentage of patients with chronic kidney disease and genetic study with alterations is higher than that described in the literature. We must carry out the genetic study of all the patients in the registry to achieve an accurate diagnosis. The diagnosis of genetic mutations in our patients has helped to diagnose their relatives.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-247 - Unexpected eGFR decline in children with CKD: deterioration in eGFR can occur at a younger age and at higher eGFR in children with bladder dysfunction

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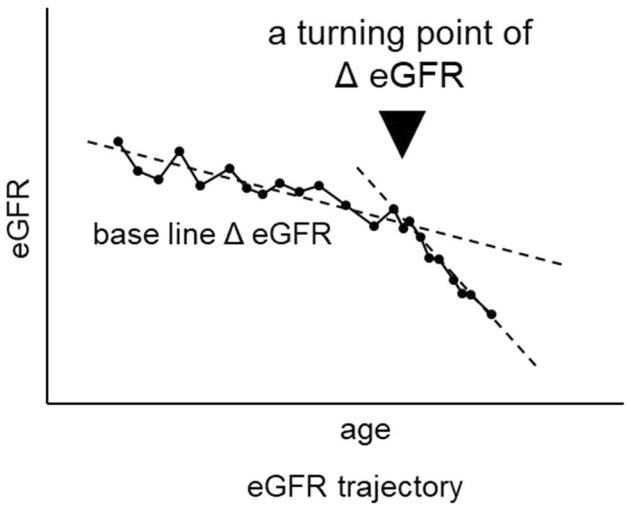
Introduction: The trajectory of the glomerular filtration rate(eGFR) usually shows an almost straight line that gradually declines. However, the rate of decline in eGFR(Δ eGFR) of some children with chronic kidney disease (CKD) may show an unexpected deterioration after a certain point. The aim of this study was to explore the potential causes that affect worsening of Δ eGFR in children with CKD.
Materials and methods: We retrospectively investigated 83 children with CKD caused by a disease that has existed since birth with eGFR trajectory records for 8 years or more. The eGFR was calculated using the creatinine-based equation for Japanese children by Uemura. The point at which the eGFR trajectory deviates from the basic straight line and begins to descend was defined as the "turning point of Δ eGFR"; frequency and clinical variables were analyzed.



Results: The turning point of Δ eGFR was observed in 39 out of 83 children. By multivariate logistic analysis, bladder dysfunction was an independent risk factor for the occurrence of the turning point of Δ eGFR after adjustment for gender, initial eGFR, and base line Δ eGFR (odds ratio 11.3; 95% confidence interval 2.14-59.5, p = 0.004). Of these 39 children, those with bladder dysfunction were significantly younger (9.5 [5.8-10.1] years vs. 11.9 [8.7-13.9], p = 0.01) and had higher eGFR (101.5 [83.2-114.9] mL/min/1.73m^2 vs. 59.7 [42.1-73.9], P < 0.001) at the time the turning point of Δ eGFR was observed than those without it.
Conclusion: In our study, children with CKD with bladder dysfunction were more likely to have an unexpected decline in eGFR, which occurred at a younger age and higher eGFR. With this in mind, children with CKD should be managed with attention to unexpected declines in eGFR.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-248 - Concordance of auscultatory office blood pressure with 24-hour ambulatory BP monitoring at different clinical thresholds in children with chronic kidney disease

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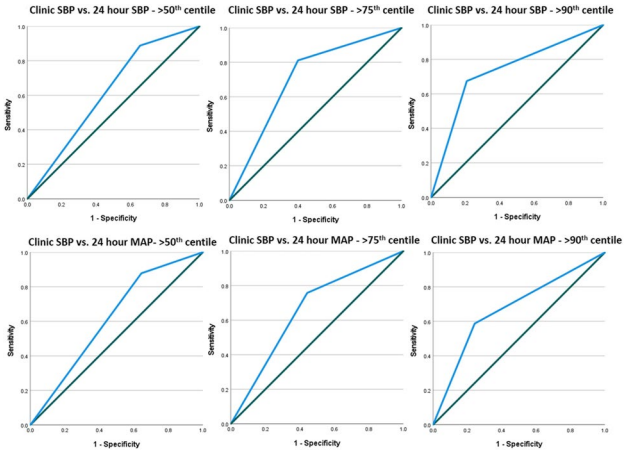
Introduction: We assess the concordance of systematically performed auscultatory office blood pressure (BP) with 24-hour ambulatory blood pressure monitoring (ABPM) in children with CKD.
Methods: Single centre study including children aged 5-18 years with predialysis stages of CKD in a dedicated hypertension clinic. At the same visit, all subjects underwent standardised auscultatory office BP (oBP) measurements (average of 3) and 24-hour ABPM. Hypertension was defined using different BP thresholds at the >50th, >75th and >90th centiles for both office and ambulatory recordings according to 2016 ESH guidelines. Concordance between oBP and ABPM readings for different thresholds was assessed using k-statistic alongside area under the applicable receiver operating characteristic curves (AUC).
Results: 245 paired measurements, including mean age 12.6±3.5 years, 53% male and eGFR 65.1±30.1ml/min/1.73m^2; 37.5% were on antihypertensive treatment. Systolic oBP was 65.7%, 51.8% and 35.1% for >50th, >75th and >90th centile thresholds respectively. On comparison with 24-hour systolic ABPM, masked hypertension rates fell from 11.4% to 7.3% and white coat hypertension increased from 13.5% to 22.4% with stricter thresholds. Agreement between oBP and ABPM assessed by k-statistic was 0.26, 0.42 and 0.46 and as assessed by AUC was 0.62, 0.71 and 0.73 for the >50th, >75th and >90th centile thresholds respectively. Similar findings were observed following comparison with 24-hour MAP.
Conclusions: In this population of children with CKD, we observed moderate agreement between office BP and ABPM. Systematically performed office BP's in our CKD population offers additive value to ABPM and improve clinical relevance when targeting lower oBP levels.

Figure 1. ROC curves for clinic SBP versus 24-hour SBP and 24-hour MAP for >50th, >75th and >90th centile thresholds. Respective AUCs were 0.62, 0.71 and 0.73 for 24-hour SBP and 0.62, 0.66 and 0.67 for 24-hour MAP.



Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-249 - Interaction of anemia and chronic kidney disease stage in the progression of the disease in children - The SP-CKDKids study

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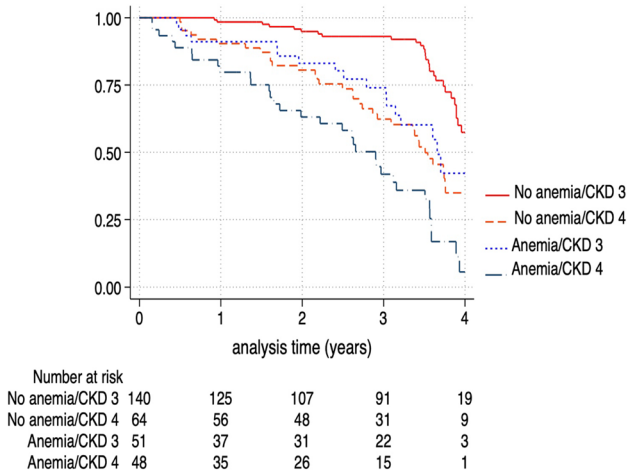
Objective: To determine whether the negative impact of anemia on the progression of chronic kidney disease (CKD) in children is modifiable by CKD stage.
Methods: Multicenter, prospective cohort study, enrolling stage 3 and 4 CKD patients with a composite endpoint of death of any cause, initiation of kidney replacement therapy (KRT), or a reduction of more than 50% in the estimated glomerular filtration rate (eGFR). The interaction term between anemia at baseline and CKD stage (3 versus 4) was modeled as a risk factor in a multivariable COX regression analysis.
Results: A total of 303 patients were enrolled in the study, with median age of 9 (5 -13) years, 60% male, and 74% had CAKUT. Ninety-nine (33%) children had anemia at baseline and 112 (37%) had an eGFR < 30ml/min/1,73m^2. Taking children with CKD stage 3 and no anemia as the reference in the regression model, the impact of anemia in CKD stage 3 children (HR=2.6, 95%CI=1.4-4.6) was comparable to CKD stage 4 children without anemia (HR=2.9, 95%CI=1.8-4.8), FIGURE 1.

Conclusion: It was already known that anemia and a more severe CKD stage are both related to a rise in morbimortality and worse outcomes in children with CKD. This study adds that there is a significant interaction between anemia and CKD stage, suggesting that the advantage of CKD stage 3 presenting a slower progression than CKD stage 4 children is lost when anemia is present. Should these results be confirmed, the treatment of anemia in early stages of CKD in children needs to be reinforced.

Figure 1 - Survival according to anemia and CKD stage



Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-250 - Impact of renal transplantation and growth hormone treatment on final height of patients with CKD

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Objective: Chronic kidney disease (CKD) patients show impaired linear growth with growth hormone (GH) being the indicated treatment. We evaluated the effect of renal transplantation (RTx) and GH treatment on FH standard deviation score (SDS) compared to height at diagnosis (HD) SDS of CKD patients.
Methods: We performed a retrospective review of medical records of patients with eGFR <45ml/min/1.73m^2. We analyzed change in height SDS from HD to FH in 4 groups: RTx patients (Group 1), RTx on GH treatment before RTx (Group 2), CKD on GH treatment without RTx (Group 3), CKD not treated with GH nor RTx (group 4).
Results: 67 patients (males:52%/females:48%) that attained FH were included (Group 1:34%, 2:28%, 3:11%, 4:27%). All patients were treated with early steroid withdrawal protocol. Mean age at diagnosis was 4.17 years and mean age at Tx was 9.5 years. Mean eGFR at diagnosis was 30ml/min/1.73m^2. Mean HD SDS was -1.39, mean FH SDS was -1.14. Mean FH SDS increased from HD SDS in group 1 from -1.6 to -0.96 (p=0.007), group 2 from -1.8 to -1.11 (p=0.05), group 3 from -1.79 to -1.47 (p=NS) and decreased in group 4 from -0.63 to -1.14 (p=NS) The SDS difference between FH and HD was significantly different in group 1 vs group 4 (+0.62 vs -0.51, p=0.005), group 2 vs group 4 (+0.65 vs -0.51, p=0.02) and group 3 vs group 4 (+0.32 vs -0.51, p=0.05). Mean height SDS just before RTx was -2.0 and increased significantly to a mean FH SDS -0.9, p<0.001 in the RTx recipients.
Conclusion: CKD patients treated with RTx and/or GH show improvement of height from diagnosis to FH and this change is significant only in RTx recipients. RTx, in the era of early steroid withdrawal protocols seems to be the optimal treatment of CKD related height deficit.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-252 - The clinical diagnosis of a nephronophthisis-like nephropathy with obvious extrarenal manifestations caused by new mutations in XPNPEP3 – case report

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Objectives: Report a case of nephronophthisis-like nephropathy with obvious extra-kidney manifestation caused by new mutations in XPNPEP3.
Methods: Review a medical report provided by Dalian Women and Children's Medical Group.
Results: An 8 years 7 months old moderate intelligent disability male was admitted to our department due to fatigue for one month, which worsened with activities. He had been admitted to the hospital two years ago for febrile convulsion, and echocardiography revealed left ventricular hypertrophy at that time. Upon admission, the results of urine and renal functions were normal. The muscle tone of both lower extremities was level IV, patellar and Achilles reflexes were slightly weak. cTnl 35ng/ml, BNP 851pg/m, which were moderately elevated. Cardiac MRI showed the left ventricle enlarged slightly, the ventricular wall thickened, the myocardium at the inferior, lateral, anterior divisions of the left ventricle was loose, and the thickness ratio of the loose area to the dense area was about 2.6 at end-systole. The whole-exon sequencing showed complex heterozygous mutations on chromosome 22 c.609 (exon4) G>A inherited from his mother, which made encoding protein shorten 305 amino acids, c.740 (exon4) A>G inherited from his father, missense mutation. Both two mutations were not included in gene database such as 1000 genomes and gnomAD. Therefore, we thought they were new mutations.
Conclusions: This patient showed atypical extrarenal manifestations with normal urine and renal function. Cardiac septal and valve defects have been reported in patients with NPHP2 and NPHP3 mutations. This is the first report about XPNPEP3 mutations resulting in cardiac defects.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-253 - The Spectrum and Changes of Biopsy-Proven Kidney Diseases in Chinese Children

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Aim: The study aimed to investigate the spectrum of biopsy-proven kidney disease in Chinese children and analyze the trend of changes.
Methods: A cross-sectional analysis of the national discharge database in China was carried out. Hospital discharge records of 21515 children under 18 years old from 238 hospitals with biopsy-proven kidney diseases from June 1, 2013, to December 31, 2018, were included. Variables included age, sex, diagnosis, year of kidney biopsy, histologic results were collected. The composition of pediatric kidney disease in different sexes, age groups, years, and clinicopathologic correlations were accessed.
Results: The glomerular disease made up 98.24%(21137/21515) of the total biopsy-proven kidney diseases. Primary glomerular disease (54.72%, 11773/21515) was the most common disease group, followed by secondary glomerular disease (40.93%, 8807/21515), and hereditary glomerular disease (2.59%, 557/21515). Among glomerular diseases, Henoch-Schonlein purpura nephritis (HSPN) (29.41%, 6216/21137) was the most frequent pathological finding among glomerular diseases, followed by immunoglobin A nephropathy (IgAN) (22.88%, 4837/21137), minimal change disease (MCD) (14.53%, 3071/21137) and lupus nephritis (LN) (11.06%, 2338/21137). Tumor (50.00%)was the most common histological finding in kidney biopsy in children less than 1-year-old. MCD (40.65%, 2303/5666) was the most comment finding among children with a diagnosis of nephrotic syndrome kidney biopsy. IgAN was the most frequent finding in children with hematuria and proteinuria(62.77%, 145/231), solitary proteinuria (33.43%, 342/1023), and solitary hematuria (60.73%, 1557/2564). The proportion of children who underwent biopsy in hospitalized children with HSPN increased from 8.77%(778/8872) in 2013 to 12.47%(1005/8060) in 2018 (p for trend <0.0001).
Conclusions: HSP and IgAN were the most prevalent diagnosis in children who underwent kidney biopsy. There was an increasing trend in HSP. This trend might be associated with a change of preference for kidney biopsy after the publications of a series of guidelines on kidney disease in China and other factors needed for further study.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-254 - Prevalence of chronic kidney disease in cyanotic congenital heart disease evaluated by serum cystatin C

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Background: Serum cystatin C is widely used as an indicator of estimated glomerular filtration rate (eGFR). Unlike serum creatinine, serum cystatin C is not affected by inflammation, protein intake, and muscle mass. Patients with congenital cyanotic heart disease (CCHD) frequently have low muscle mass and chronic inflammation. This study aims to compare the prevalence of CKD between using serum cystatin C and serum creatinine to calculate eGFR and to determine factors associated with CKD in pediatric patients with CCHD.
Method: A prospective cross-sectional study was conducted from July 2019 to October 2020. Pediatric patients with CCHD aged 1 to 18 years at Chiang Mai University hospital were enrolled. Serum cystatin C was evaluated by ELISA kit. eGFR was calculated by Cystatin C-based CKiD equation. The correlation and agreement between eGFR from creatinine and cystatin C were determined. We compared the prevalence of CKD in patients with CCHD determined by creatinine and cystatin C-based eGFR. The Binary logistic regression analysis was used to identify the risk factors for CKD.
Results: 30 patients with CCHD were enrolled in this study. The prevalence of CKD calculated from serum cystatin C and serum creatinine-based eGFR were 14/30 patients (46.7%) and 8/30 patients (26.7%), respectively. eGFR calculated by serum creatinine was significantly correlated with eGFR calculated by serum cystatin C (r=0.66, $p< 0.001$). The Bland-Altman analysis quantified a good agreement between two eGFR measurements. However, the mean difference between the two methods (16.45±20.23 ml/min/1.73m^2) was high, affecting the assessment of the prevalence of CKD. Albuminuria was significantly correlated with lower eGFR (p <0.001). Hematocrit level was an associated factor for CKD(p=0.05, OR=6.23).
Conclusion: eGFR calculated by serum creatinine underestimates chronic kidney disease (CKD) recognition. Albuminuria was found to be associated with lower eGFR. High hematocrit level is the risk factor for CKD in this study.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-255 - A retrospective analysis of renal outcome and prognostic factors in childhood renal tumors

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Background: Considering the tumor site and the details of the treatment including unilateral nephrectomy, childhood renal cancer survivors are predicted to have a higher risk of chronic kidney disease (CKD). However, there are few reports on their actual renal outcome and major prognostic factors of impaired renal function.
Methods: We retrospectively analyzed cumulative incidence of CKD in a cohort of 31 children with renal tumors who were treated at Hyogo Prefectural Kobe Children's Hospital in Japan between 1998 and 2018. We registered patients' age, height, histology, details of treatment, compensatory hypertrophy of the residual kidney with ultrasonography, urine findings, and renal function during follow-up. Renal function was evaluated with estimated glomerular filtration rate using creatinine-based equation for Japanese children and adolescents.
Results: In the 31 patients who met the inclusion criteria, the median age at diagnosis was 2.8 years. The median observation period and age at last visit were 9.9 years and 12.8 years, respectively. Thirty of the cases affected unilaterally and all patients were surgically treated with total unilateral nephrectomy. The percentages of patients who received chemotherapy and radiation therapy of whole abdominal irradiation were 90.3 % and 54.8 %, respectively. The cumulative incidence of CKD was 63.5% and all of them were CKD stage 2. Univariate analyses revealed that patients with radiation therapy and those without compensatory hypertrophy of the residual kidney were significantly more common in CKD patients, while radiation therapy was the only prognostic factor that significantly affected renal function with multivariate analysis.
Conclusions: The cumulative incidence of CKD in childhood renal cancer survivors is high, which requires longer-term follow-up of renal

function. Special attention should be paid to renal function in children with radiation therapy.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-256 - A case of TSC2/PKD1 contiguous gene syndrome: treatment for neurological complications would improve the management of kidney complications

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Introduction: TSC2/PKD1 contiguous gene syndrome (PKDTS) is caused by deletion of the TSC2 and PKD1 genes on chromosome 16. Deletions inactivating both genes are associated with the clinical manifestations of tuberous sclerosis complex (TSC) and polycystic kidney disease (PKD). PKDTS causes more severe intellectual and cognitive disabilities and earlier-onset kidney failure than typical TSC.
Case report: The patient was a 23-year-old female with PKDTS, who has been diagnosed through array comparative genomic hybridization (deletion of 190 kb on chromosome 16 including *TSC2* and *PKD1* genes). PKD was detected on fetal ultrasound. At 1 year of age, she was clinically diagnosed with TSC based on infantile spasm, multiple cortical tubers in the brain, and hypopigmented macules. At 4 years, she developed refractory epileptic seizures, which were not controlled by antiepileptic agents, and her mental development gradually became delayed. At 15 years, angiomyolipoma was detected; however, her kidney function remained normal. At 17 years, she fell and hit her lower back due to epileptic seizures, which resulted in kidney cyst bleeding and her kidney function began to worsen. After her kidney dysfunction progressed, we started everolimus for angiomyolipoma; however, her kidney function continued to decline. At 23 years, she had additional two kidney cyst bleeding episodes due to epilepsy and her kidney dysfunction progressed to kidney failure. We started hemodialysis with a permanent catheter, although we were concerned about her epilepsy and impulsive behavior during hemodialysis. Fortunately, she underwent hemodialysis safely with some supports by her parents and medical team. Nephrectomy and living donor kidney transplantation are planned.
Conclusion: In PKDTS, neurological complications of TSC adversely affect kidney complications and limit treatment options. Lately, earlier induction of everolimus has been demonstrated to improve neurological complications of TSC. Treatment for neurological complications by everolimus would improve the management of kidney complications in PKDTS.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-257 - Efficacy and Safety of Dapagliflozin in Children With CKD 1-4 without Diabetes

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Single studies show the possible effectiveness of SGLT2i in children with proteinuria. The clinical model for imitating the intake of SGLT2i in children is renal glycosuria, which does not bring significant suffering to the kids.
The aim of the study was to evaluate the safety and efficacy of SGLT2i in children with CKD 1-4 stages.
Materials and methods: A prospective randomized trial with POEM design started in 2020 as an open out of label study was conducted in 26 children (6-18 years old) with CKD presented by albuminuria (+/- hematuria) 283±10.1 mg/L. All children have been already receiving an ACE inhibitor or ARB to control albuminuria.
The following criteria for assessing the safety of SGLT2i were selected: assessment of the child's clinical condition, blood pressure, decrease in eGFR, and development of urinary tract infections. The effectiveness of dapagliflozin 0.125 mg/kg in one dose was carried out according to the albuminuria trend.
Results and discussion: Dapagliflozin has been shown to be well-tolerated and safe. Clinical complaints in the form of transient weakness were documented in 4 children (15%), a decrease in blood pressure by 5-10 percentiles in 5 (19%), a transient decrease in eGFR by 4±1 ml/min in 7 children (26%) with worsening of kidney function in CKD 4. Efficiency in reducing albuminuria was demonstrated in 19 children (73%).
The addition of SGLT2i to ACE inhibitor / ARB therapy reduced albuminuria from 283 ± 10.1 mg / L to 156 ± 8 mg / L (P≤0/01).
Conclusions: The data obtained prove the efficacy and safety of dapagliflozin/iRAS in children with CKD 1-3 with conflicting results in CKD 4 with minimal effect on erythrocyturia in all cohorts.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-258 - Nutrition-focused physical examination (NFPE) for predicting risk of protein energy wasting (PEW) in children with chronic kidney disease and those on dialysis

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There is a need to explore less laborious point- of-care assessment tools to predict risk of protein energy wasting (PEW) in children with CKD.This cross-sectional study was undertaken to assess the profile of specific nutrition-focused physical examination (NFPE) and mid-arm muscle area(MAMA) in children with CKD and determine their role in the diagnosis and risk prediction of PEW.
Methods: PEW criteria was applied to all eligible children and MAMA was derived from mid arm circumference and triceps skin fold thickness. NFPE signs examined were muscle wasting (MW) and subcutaneous fat loss(FL).
Results: One twenty six children with CKD (86 in CKD stage 2-4 and 40 on dialysis) were studied. PEW was prevalent in 41.8% children with CKD2-4 and in 72.5% on dialysis. In children with CKD2-4, low MAMA, MW and FL were good risk predictors of PEW with an odd's ratio of 5.3(1.55,18.30), 10.6(3.8,29.8) and 10.5(3.7,29.2) respectively (p=<0.001). In children on dialysis,

low MAMA, MW and FL were good risk predictors of PEW with an odd's ratio of 17(2.2,127.7);p=0.017, 16.6(3,90.8);p=0.001 and 19(2.1,170.3);p=0.009 respectively (Table). MW demonstrated high sensitivity and specificity [80.6% and 72% respectively with a positive predictive value(PPV) of 67.4%] to diagnose PEW in the CKD2-4 group and in those on dialysis [86.2% and72.1% respectively with PPV of 89.3%].

Conclusion: Clinical signs based on NFPE are useful in predicting risk of PEW in children with CKD2-4 and in those on dialysis. In addition, physical signs of muscle wasting and subcutaneous fat loss have a diagnostic ability to identify children with PEW in both groups. These findings reiterate the importance and relevance of NFPE in the assessment of children with CKD. Besides, NFPE has the potential to be instituted by trained nurses and dieticians as a point of care assessment for PEW in any health care context.

Table: MAMA and NFPE parameters (MW: muscle wasting; FL: Subcutaneous fat loss) as risk predictors for PEW in children with CKD2-4 and on dialysis. PEW-(PEW absent) PEW+ (PEW present)

Parameters	CKD2-4 (n=86)				Dialysis (n=40)			
	PEW-	PEW+	OR (95% C.I)	p value	PEW-	PEW+	OR (95% C.I)	p value
MAMA n(%) n=83								
<5th centile	3(6.1)	16(47.0)	5.3(1.55,18.30)	<0.001	1(9.0)	17(58.6)	17(2.2,127.7)	0.017
>5th centile	46(93.8)	18(52.9)	Ref		10(90.1)	12(41.3)	Ref	
MW n(%) n=86								
Absent	36(83.7)	7(16.2)	10.6(3.8,29.8)	<0.001	8(66.7)	4(33.3)	16.6(3,90.8)	0.001
Present	14(32.5)	29(67.4)	Ref		3(10.7)	25(89.2)	Ref	
FL n(%) n=86								
Absent	42(77.7)	12(22.2)	10.5(3.7,29.2)	<0.001	10(50)	10(50)	19(2.1,170.3)	0.009
Present	8(25)	24(75)	Ref		1(5)	19(95)	Ref	

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-259 - Body cell mass measurement by whole-body potassium counter in children with chronic kidney disease – a longitudinal observational study

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Nutritional assessment in children with chronic kidney disease (cCKD) using anthropometry is confounded by edema and overhydration. Body cell mass (BCM), an ideal measure of functional nutritional status could serve as a reference measure for comparison with anthropometry. The method of choice for measuring BCM is the whole body potassium counter (WBPC) which is insensitive to major fluid shifts. The objective of this study is to determine BCM using WBPC in cCKD at baseline and follow up, and to explore its association with body mass index(BMI).

Methods: Fifty children (age 1-18yrs) in CKD stages2-5D with normokalemia, and 20 healthy children as reference underwent BCM measurement by WBPC. Body segments were scanned for 30mins by WBPC (4 NaI detectors captured y rays emitted by ^{40}K). Total body potassium(TBK gm, meq/kg), BCM (kg) and BCMI (indexed to gender-based height) were determined. BCM was measured twice at 3-6monthly interval in cCKD. BMI for height-age was estimated and expressed as z scores (BAZ).

Results: Comparing cCKD (24 on dialysis, 74% males, mean age 128.3 ± 38.4mn) with controls (55% males,mean age 143.3 ± 43.1mn),the mean BCMI was significantly lower in cCKD [4.02 ± 1.03 vs 4.85±1.19; p= 0.005 respectively] with 50th centile BCMI of controls corresponding to 80thcentile BCMI in cCKD. The mean BCMI was significantly lower in those on dialysis compared to those pre-dialysis [3.70 ± 0.84 vs 4.31 ± 1.11, p=0.034]. In cCKD, BAZ correlated with BCMI at baseline (Figure; r= 0.61, p<0.001) while delta change in BAZ and BCMI correlated at 13months median follow up (r=0.53, p<0.001).

Conclusion: Measurement of BCM using WBPC revealed significant differences in BCMI between cCKD, those on dialysis and controls. Though preliminary findings suggest BMI to be a probable surrogate measure of BCMI in cCKD, validation of different nutritional assessment tools to predict BCM measured by WBPC is required.

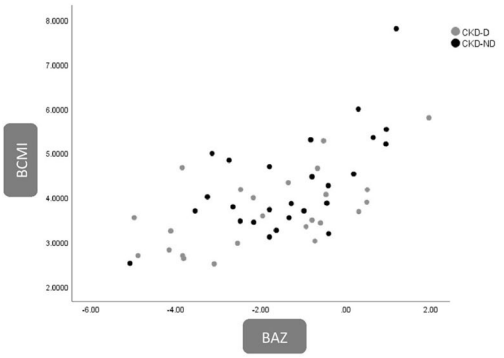

Figure: Correlation of BMI z scores (BAZ) with body cell mass index (BCMI) (r=0.61, p<0.001) in children with CKD (CKD-D: On dialysis; CKD-ND: non-dialysis).

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-260 - GATA3 associated hypoparathyroidism, deafness, and renal dysplasia (HDR) syndrome masquerading as idiopathic infantile hypercalcemia

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Background: Idiopathic infantile hypercalcemia (IIH) is caused by defective vitamin D degradation due to 24-hydroxylase (*CYP24A1*) deficiency or decreased renal tubular phosphate reabsorption due to sodium phosphate co-transporter NaPi-IIa (*SLC34A1*) mutation with low serum parathyroid hormone (PTH) levels.

Aims: To describe an infant with hypercalcemia and IIH-like clinical presentation who was found to have a damaging mutation in *GATA3* but other relevant variants.

Case history: A male infant of non-consanguineous, healthy parents was evaluated for antenatally detected urinary tract dilation. Imaging

studies revealed left renal hypoplasia, bilateral grade III vesico-ureteral reflux with tortuous left duplex ureter, no evidence of nephrocalcinosis, and normal bladder. He initially failed, but later passed the newborn hearing screen. He was fully breast-fed and supplemented with 400 IU vitamin D. He was irritable, with a gaseous abdomen and mild constipation, but gained weight along the 50th centile. He had moderate hypercalcemia and hypercalciuria. PTH was suppressed, 25-OH D3 was normal and 1,25 (OH)2 D3 concentrations were high. Infantile idiopathic hypercalcemia was suspected. Vitamin D supplements were stopped, followed by gradual normalization of serum calcium, urine calcium excretion and PTH (Table 1). Whole exome sequencing identified a heterozygous pathogenic frameshift variant in *GATA3*; c.708del / p.(Ser237Alafs*29).

Discussion: Pathogenic variants in *GATA3*, a dual zinc finger transcription factor, expressed in developing parathyroid, inner ear and kidneys, cause hypoparathyroidism, (sensorineural) deafness, and renal dysplasia (HDR syndrome; MIM# 146255). Primary hypoparathyroidism is typically associated with hypocalcaemia. The clinical phenotype is variable, and appearance of each of the principal features accumulates with age. Yet, presentation with hypercalcemia is unexpected.

Conclusions: We report an unusual presentation of HDR syndrome in an infant boy due to GATA3 haploinsufficiency under the disguise of idiopathic infantile hypercalcemia associated with elevated 1,25 (OH)2 D3 concentrations. Moderate hypercalcemia may not exclude an early diagnosis of HDR syndrome.

Age	Calcium	PTH	25-OH	1,25 (OH)2	U Ca/Cr	Vit D
	9.0-11.0	6.4-88.6	30-100	19.9-79.3	< 0.81	Suppl
months	mg/dL	pg/mL	ng/mL	pg/mL	g/g	daily
1.6	11.4	< 4.0	55.0	163	1.435	400 IU
2.9	10.9		51.0	-	-	off x 5 weeks
3.7	10.7	< 4.0	-	-	0.962	-
4.8	10.5	17	38.0	86.6	0.507	-
7.5	10.1	27.7	21.2	79.8	0.383	-

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-261 - Long noncoding RNA uc.412 promotes glomerulosclerosis via binding ELAVL1 in chronic kidney disease

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Introduction: Glomerulosclerosis is a characteristic pathological feature of chronic kidney disease (CKD). Evidence indicates that mesangial cells (MCs) play a critical role in this process. However, their exact mechanism of action remains unclear. Using RNA-seq analysis, we previously found that lncRNA uc.412 is involved in MC proliferation. Here, the effect of uc.412 on glomerulosclerosis and its potential mechanism were explored.

Methods: *In vivo*, 5/6 nephrectomy was performed to establish CKD mouse models. LncRNA uc.412 expression and renal fibrogenesis in CKD models were evaluated. *In vitro,* the MCs were treated with TGF-β1 (2 ng/mL) to observe ECM production and uc.412 expression.

Results: We found that the expression of uc.412 was significantly increased in CKD mice and was induced by TGF-β1 via Smad3-dependent signaling. Overexpression of uc.412 caused extracellular matrix (ECM) generation in MCs and knockdown of uc.412 alleviated TGF-β1-induced MC ECM accumulation. Using RNA pull-down analysis, we found that ELAVL1 was the specific binding protein for uc.412. ELAVL1 expression was increased in TGF-β1-treated MCs and silencing of ELAVL1 expression attenuated ECM accumulation.

Conclusion: Thus, we demonstrated that uc.412, which is regulated by a Smad3-dependent mechanism, is significantly increased during CKD progression via regulation of ELAVL1 expression. Our findings provide a novel therapeutic strategy for CKD treatment.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-262 - Quest of biomarkers to predict the progression of chronic kidney diseases in children with CAKUT of Korea; a report from KNOW-Ped CKD

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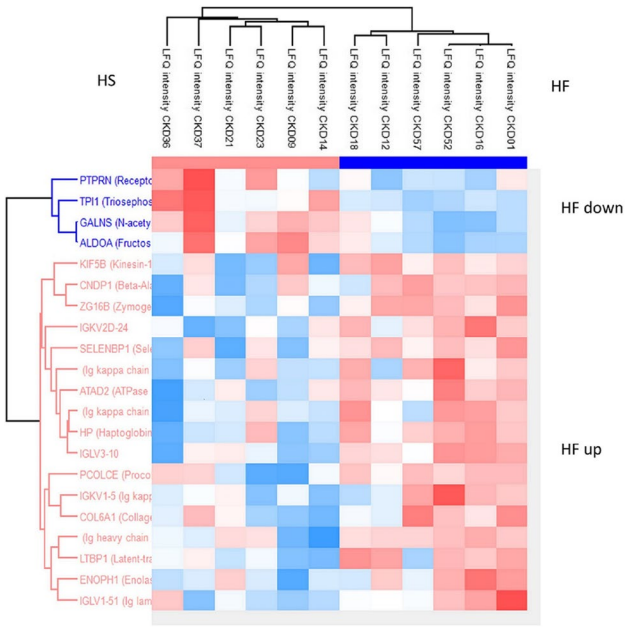
Introduction: Chronic kidney diseases (CKD) often progress to end-stage kidney disease. However, the progression rate of CKD varies among patients, especially in children. A significant number of pediatric CKD are caused by congenital anomalies of the kidney and urinary tract (CAKUT), and its progression is hard to predict. Here, we report our search for urinary biomarkers to predict the progression of CKD in this population.

Methods: We selected 25 patients with CAKUT (kidney hypoplasia (H, n=12) or reflux nephropathy (R, n=13)) from the pediatric prospective cohort study KNOW-Ped CKD (KoreaN cohort study for outcomes in patients with pediatric CKD), and grouped into the fast (F) and slow (S) progression groups (an annual eGFR decline ≥ 5 mL/min/1.73 m^2 vs. < 5 mL/min/1.73 m^2). Baseline characteristics of eGFR, proteinuria, hypertension, and age were comparable between the groups. Urine samples were analyzed using capillary electrophoresis-mass spectrometry.

Results: In total, 2,041 proteins were identified, and 71 as the 1st targeted proteins (valid value > 70%, permutation FDR < 0.05, log2 fold change ± 1.5). In the RF group, 45 proteins including epidermal growth factor, collagen type XIV α1 chain, tenascin-X, and Ephrin type-B receptor 4 were significantly down-regulated compared with the RS group. Five proteins including Apolipoprotein A-II more abundant in the RF group. In the HF group, four proteins including Triosephosphate isomerase were significantly down-regulated, and 17 proteins, including the collagen type VI α1 chain were up-regulated than the HS group. In biological pathway analysis, angiogenesis pathway was deactivated in the RF group. The collagen catabolic process and polarized epithelial cell differentiation pathway were activated in the HF group, whereas NADH regeneration and glycolytic process were associated with slow progression.



Conclusions: We found several differentially regulated peptides according to progression rate and underlying diseases. Upon validation, these might be candidates of biomarkers predicting the progression of CKD.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-263 - Life participation in children with CKD: Impact on school attendance, social interests and sport participation

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Background: Children with Chronic Kidney Disease (CKD) face greater barriers in life compared to their peers. Living with CKD impacts on various life domains, including school, social participation, and sporting involvement. Our study aimed to quantify the impact of CKD on a child's school attendance, sport participation and social activities. We also investigated the impact of stage of CKD on these domains of life participation.

Methods: This cross-sectional study used data from the kids with CKD study, which recruited children from five paediatric nephrology units across Australia and New Zealand. Participants aged 6-18 years old with CKD were recruited between 2013 and 2016. Data on school attendance, social activities and sport participation was obtained from patient and parent questionnaires. The relationship between CKD stage was investigated using Poisson regression.
Results: The median number of days children with CKD missed in the preceding four weeks of school was two days (IQR: 0-6). Children on dialysis missed 4 fold higher days of school and children with a kidney transplant missed 2 fold higher days of school compared to children with CKD stages 1-2. The top 5 sports children with CKD participate in are swimming (17%), soccer (17%), football/rugby (12%), dance (9%), and basketball (8%). The median number of sports played by children with CKD was one (IQR: 0-2). Compared to children with CKD stages 1-2, children on dialysis played 47% (95% CI: 21%-65%) fewer sports and children with a kidney transplant played 23% (95% CI: 2 %-39%) fewer sports.
Conclusion: Children with CKD play similar sports to their peers but children receiving kidney replacement therapy played fewer sports compared to children with CKD stages 1-2. Strategies are needed to improve school attendance and sport participation among children with CKD.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-264 - A two years slope of glomerular filtration rate is relevant to predict the progression of chronic kidney disease in children – The SP-CKDKids study

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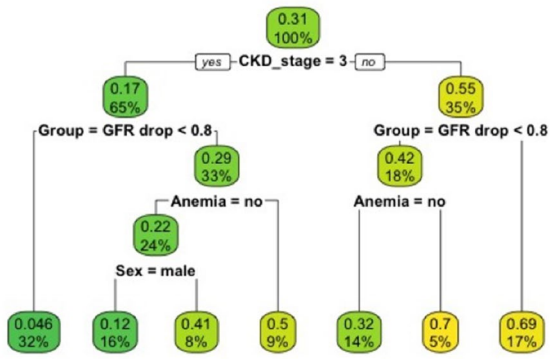
Objective: To test whether the 2-year eGFR slope over time is predictive of CKD progression in children.
Methods: Multicenter prospective cohort involving children with CKD stage 3-4. The outcome was dialysis or transplantation during follow-up, and the main explanatory variable was the 2-year baseline eGFR slope. Covariates included age, sex, CKD etiology, disease stage, proteinuria, anemia, and arterial hypertension (AH). Also, the occurrence of emergency room visit/hospitalization during the baseline was added to adjust for acute illnesses on the eGFR slope. The association of risk factors with the outcome was modeled through two different machine learning algorithms: Cox regression, and a decision tree model.
Results: The study involved 206 children aged 8.0 (4.5 to 12.6) years, 61% male, 73% CAKUT, 65% CKD stage 3. During 2.2 (2.1 to 2.4) years of baseline, children attended to a median of 5 visits, and the eGFR dropped by 3.4 ml/min/1.73. Median eGFR slope was a drop of

-0.8 (-2.1 to 0.5) ml/min/1.73/visit. Accordingly, children were categorized as G1: drop ≤0.8 and G2: drop >0.8. Subsequently, the sample was followed for an additional 4.3 (3.0 to 6.4) years and kidney failure occurred in 63 cases (31%). Adjusted COX model revealed that CKD-Stage 4 [HR 5.5 (3.2 to 9.3)], drop>0.8 [HR 4.3 (2.5 to 7.5)], and AH [HR 1.9 (1.2 to 3.2)] were independently associated with the outcome. The decision tree model revealed that the eGFR drop>0.8 was the second most important variable to predict the outcome (FIGURE 1).
Conclusions: The main finding of this study is the association of the 2-year eGFR slope with CKD progression to kidney failure in children. This result confirms previous studies in adults suggesting that eGFR slope over time may be a piece of relevant information, either as a risk factor, or a surrogate endpoint in clinical trials.

FIGURE 1 – Decision tree to depict the risk factors for the outcome (dialysis or transplantation) in CKD children.



All branches to left represent *yes*
Importance of risk factors: CKD stage: 6.6, GFR drop: 3.1, Anemia: 2.4, Sex: 1.7

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-266 - Rate of progression and its risk factors in pediatric chronic kidney disease: A cohort study

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Background: There is paucity of information regarding the clinical course of pediatric chronic kidney disease (CKD) from India.
Objectives: The objectives of this cohort study were to evaluate the etiology of CKD in children at our center, assess the co-morbidities, and identify the risk factors and the rate of progression of CKD.
Methods: Children aged 2-18 years with CKD stages 2-5 (KDIGO guidelines) were enrolled. The etiology of CKD and its co-morbidities were recorded. Kaplan-Meier survival curves were used to analyze the time to progression of CKD.
Results: Out of the 200 patients enrolled, the number of patients belonging to CKD 2, 3a, 3b, 4 and 5 were 48 (24%), 17(8.5%), 23 (11.5%), 30 (15%) and 82 (41%) respectively. The etiologies of CKD included congenital anomalies of kidney and urinary tract (CAKUT) [109 (54.5%)], chronic glomerular diseases [31(15.5%)], and cystic renal disease [19 (9.5%)]. The co-morbidities associated with CKD included CKD-MBD [164 (82%)], metabolic acidosis [159 (79.5%)], hypertension [144 (72%)], anemia [128 (64%)], and growth retardation [110 (55%)]. Early stages of CKD (CKD 2 & 3a) were often complicated by anemia [23 (35.3%)], CKD-MBD [37(56.9%)], short stature [28 (43.1%)] and hypertension [40 (61.5%)].The median (IQR) duration of follow-up of the cohort was 20 (12,30) months. The median decline in the rate of eGFR was 1.6mL/min/1.73m2/yr. On multivariable analysis, proteinuria (Hazard ratio-3.5 (95%CI 1.4,8.8) p-value 0.01) and hyperphosphatemia (Hazard ratio-2.2 (95%CI 1.1,4.3) p-value 0.03) were significant predictors for progression of CKD.
Conclusions: CAKUT was the commonest cause of CKD in our cohort and the median decline in the rate of eGFR was 1.6mL/min/1.73m2/yr. Even the earlier stages of CKD were complicated by major comorbidities. Proteinuria and hyperphosphatemia were risk factors for progression of CKD.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-268 - Serum apolipoproteins (apoA-1, apoB and apoB/apoA-1 ratio) for early identification of dyslipidemia in children with CKD

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Background: Dyslipidemia in children with CKD is identified based on lipid profile parameters; changes in lipoprotein quality precede quantitative changes.
Aims & Objectives: The primary objective of the study was to determine prevalence of dyslipidemia and estimate levels of apoB, apoA-1 and ratio of apoB/apoA-1 in children and adolescents (2-18 years) with CKD (all stages).
Methods: A cross-sectional study was done from January-October 2021; overweight, obese children, known cases of diabetes mellitus, hypothyroidism or on steroid therapy or lipid lowering drugs were excluded. Clinical details were elicited and examination done. Besides hemogram, KFT, VBG, Total cholesterol, LDL-C, triglycerides, HDL-C, apoA-1 and apo-B were estimated to identify dyslipidemia. Relevant tests of significance were applied and ROC curves were drawn for apoA-1, apoB and apoB/apoA-1 ratios.
Results: 76 (61M: 15 F) children with median (IQR) age 7 (3.25-11) years were enrolled; undernutrition was present in 31.6% and stunting in 27.6%. Dyslipidemia was seen in 78.9% with a prevalence of 71.7% in early and 95.7% in later stages of CKD (P=0.02). The median (IQR) values of apoB, apoA-1, and apoB/apoA-1 ratio were 78 (58-110) mg/dl, 80 (63-96.75) mg/dl, 0.88 (0.68-1.41) respectively; apoB, apoA-1 and apoB/apoA-1 ratio had a sensitivity of 26.67%, 86.67% and 70% and specificity of 87.5%, 62.5%, 62.5% respectively for diagnosis of dyslipidemia. The ROC of apoB, apoA-1 and apoB/apoA-1 ratio showed AUC of 0.66, 0.68, 0.74 (P= 0.4, 0.02, <0.01) respectively.

Conclusion: The prevalence (78.9%) of dyslipidemia was high in patients with CKD especially in those with later stages. The ratio of apoB/apoA-1 was altered early and appears to be promising for early detection.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-269 - Correlation of Fibroblast Growth Factor 23 with left ventricular hypertrophy in children with chronic kidney disease

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ABSTRACT
Background: Decreased glomerular filtration rate in chronic kidney disease (CKD) patients, change in calcium and phosphate homeostasis. High phosphate levels will stimulate the secretion of Fibroblast Growth Factor 23 (FGF23). High FGF23 levels potentially cause cardiovascular disease (CVD), including left ventricular hypertrophy (LVH) Mortality in children with CKD, is 30 times higher than in the general population, which CVD being known as the main cause.
Objective: To know the relationship between FGF23 with LVH in CKD children.
Methods: The study design was cross-sectional, carried out in BONA I ward and Pediatric Nephrology Outpatient Clinic of Dr. Soetomo Hospital Surabaya, during December 2019-March 2020. Involving children with CKD stage 1-5, aged 3 months-18 years old, and parents willing to join the research. Children on phosphate-binder, vitamin D therapy, or severely ill were excluded. The blood level of FGF23 is checked. Echocardiography was performed to determine LVH.
Results: A total of 52 CKD stage 1-5 children were involved, the mean age was 11.44 years old, and 50% were boys. The most common cause of CKD was glomerulonephritis in 63.4%. Degree of CKD were related to FGF23 (r_s=0.834; p=0.000). The incidence of LVH was 48.1%. FGF23 levels were associated with LVH (p=0.000). High levels of FGF23 were associated with LVH (Phi=0.695; p=0.000).
Conclusion: FGF23 levels were associated with left ventricular hypertrophy in chronic kidney disease children.
Keywords: Chronic kidney disease, cardiovascular disease, FGF23, left ventricular hypertrophy.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-270 - Short term efficacy and safety of atorvastatin for dyslipidemia in children with chronic kidney disease (CKD) stage 2-5

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Background: Dyslipidemia is a potentially modifiable risk factor in patients with chronic kidney disease. Information on efficacy and safety of statins in pediatric CKD is limited.
Aims and objectives: Proportion of patients achieving target lipid levels of LDL-C ≤100 mg/dL and non-HDL-C ≤120mg/dL at 24 weeks.
Methods and materials: Patients with CKD stage 2-5, aged 5- 18 years with low density lipoprotein cholesterol (LDL-C) >130mg/dL and/or non-high density lipoprotein cholesterol (HDL-C) >145mg/dL were enrolled from September 2019 to February 2021. All patients were administered atorvastatin 10 mg/day, that was escalated to 20 mg if LDL-C>100 mg/dL at 12 weeks. Tests for significance within or between groups included Wilcoxon signed rank and rank sum test.
Results: Of the 31 patients enrolled, two-thirds were in the age group of 13-18 years (67.7%). Boys constituted 71% of the cohort and 64.5% had CKD stage II with 71.0% having nephrotic range proteinuria. Target lipid levels were achieved in 45.2% patients (95% CI 27.8%-63.7%) at 24-week; 22 patients required dose escalation to 20 mg at 12 weeks. There was no difference in median reduction in lipid levels with 10 mg/day (n=9) versus 20 mg/day (n=22; p=0.3). Higher baseline LDL-C (OR 1.06, 95% CI 1.00 to 1.11) and older age (OR 36.50 95% CI 2.57 to 519.14) were independent predictors of failure to achieve target lipid levels with 10 mg/day atorvastatin. None had persistent rise in AST/ALT levels >3 times upper normal limit (UNL) or CPK >10 times UNL. No differences were noted in the adverse effects of atorvastatin 10 mg/day and 20 mg/day.
Conclusion: Atorvastatin (10-20 mg/day) administered for 24 weeks was safe and effectively reduced LDL-C and non HDL-C in children with CKD stage 2-5. Patients with higher baseline LDL-C required higher doses to achieve the target.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-271 - The Effects of 12 weeks Contact-free Combined Exercise Program on Health Fitness, Quality of Life, Physical activity and Kidney Function in Pediatric Patients with Chronic Kidney Disease

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Background: Children with chronic kidney disease (CKD) experience poor physical functioning, muscle wasting, and reduced cardiac functioning, which contribute to poor health fitness. Previous studies revealed regular physical activity improved exercise capacity and muscle strength in adults with CKD. Maintaining regular physical activity and exercising routinely in a home environment is an important strategy for a healthy life during the coronavirus crisis. The aim of this study is to assess the efficacy of a contact-free exercise program on health fitness, QOL and kidney function in children with CKD.
Methods: This prospective experimental study was conducted between June 2021 and August 2021, during the COVID-19 pandemic period. The contact-less combined exercise program consisted of aerobic and resistance training for 12 weeks at home. Participants had a live streaming class with the instructor once a week, watched and followed the recorded exercise video twice a week. Health-related fitness, physical activity level, QOL, and laboratory data

were evaluated before and after the intervention. Health-related fitness measures included grip strength, sit-up test, sit and reach test, progressive aerobic cardiovascular endurance run.
Results: Fourteen children with CKD (male:female=13:1) enrolled at the median age of 13.5 (interquartile range (IQR) 13-15.8) years and five (35.7%) of them were on dialysis. After 12 weeks of the exercise program, all health-related fitness measures showed significant improvement (P <0.05). The median physical activity level reported by the questionnaire significantly increased from 861 (IQR 527-1357) to 2538 (IQR 2190-3302) (P =0.011). In patient self-reports, patients had better QOL after exercise program in physical, emotional, and social functioning categories. While blood urea nitrogen and low-density lipoprotein levels were decreased in predialysis CKD patients after exercise, serum creatinine was increased in patients with dialysis.
Conclusions: A contact-free combined exercise program can effectively improve health fitness, physical activity, and QOL in pediatric CKD patients.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-272 - Treatment with calcimimetic AMG 416 improves high phosphate diet-induced cardiac dysfunction in mice

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Objectives: Hyperphosphatemia enhances the synthesis of the phosphaturic hormones parathyroid hormone (PTH) and fibroblast growth factor (FGF) 23, thereby promoting cardiovascular (CV) morbidity and mortality. In the secondary analysis of the EVOLVE trial, the calcimimetic cinacalcet significantly reduced PTH and FGF23 levels in hemodialysis patients and the latter was associated with lower rates of CV events and death. Administration of the intravenous calcimimetic etelcalcetide (AMG 416) resulted in suppression of FGF23 and improvement of left ventricular (LV) hypertrophy progression in hemodialysis patients. Whether AMG 416 has cardioprotective properties in high phosphate diet-induced cardiac dysfunction is unknown.
Methods: After four months on a 2% high phosphate diet (HPD), male C57BL/6N were treated with AMG 416 (1 mg/kg per day) via osmotic mini pumps for another two months and compared to mice on HPD treated with vehicle or receiving a 0.8% normal phosphate diet (NPD). Cardiac function was evaluated by echocardiography before start and at the end of therapy and parameters of mineral metabolism were determined.
Results: AMG 416 lowered HPD-induced FGF23 and PTH levels by 80% and 75%, respectively and resulted in a 17% reduction of serum calcium levels compared to the respective controls. AMG 416 did not affect HPD-enhanced serum phosphate levels and phosphaturia. HPD resulted in a dilatated cardiac phenotype characterized by increased LV diameter, reduced anterior and posterior wall thicknesses, increased end-systolic and end-diastolic volumes, and consequently impaired ejection fraction and fractional shortening. LV dilatation and systolic dysfunction were prevented by concomitant AMG 416 treatment. On cellular level, the HPD significantly increased cardiomyocyte cross-sectional area, whereas the AMG 416 treated group only showed a non-significant increase compared to NPD.
Conclusions: Treatment with AMG 416 suppresses FGF23 and PTH levels in HPD-fed mice without altering hyperphosphatemia, and effectively inhibits HPD-induced LV dilatation and systolic dysfunction despite concomitant mild hypocalcemia.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-275 - Renal papillary necrosis - an under-recognized complication of sickle cell disease

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Sickle cell disease (SCD) is a group of hemoglobinopathies that can lead to sickling and vaso-occlusion. Renal papillary necrosis (RPN) and renal infarction are underrecognized complications of SCD that are not commonly seen in the daily practice but that can have severe consequences when its diagnosis is delayed.
A 13-year-old male with SCD with SS homozygosity was referred to the emergency department and admitted for painless, macroscopic hematuria over the course of that day. He denied fever, dysuria or pollakiuria or abdominal pain. Three weeks prior to the onset of hematuria, he was hospitalized for a vaso-occlusive crisis and was medicated with NSAIDs for 7 days. On physical examination he presented slightly discolored conjunctivae, the abdomen was soft, nontender with no organomegaly. He was normotensive and had normal heart rate. The blood work showed: hemoglobin 10,3 g/dL, urea 25 mg/dl, creatinine 0,55 mg/dl and normal coagulation tests. Urinalysis showed 70 mg/dL protein, >50 red blood cells and 2-5 leucocytes per high-power field. Urine culture was negative. Renal ultrasound followed by tomography urogram was performed which identified a hypovascular nodulariform area in right the kidney upper pole and a slight indentation of the papillae of some caliceal groups, supporting the diagnosis of renal infarction and papillary necrosis. Hyperhydration with IV fluids, urine alkalinization and bedrest was maintained until hematuria cleared up, after 4 days. Two weeks after discharge, at follow-up visit, he was asymptomatic with no proteinuria or hematuria on urinalysis.
Sickle cell nephropathy is a common condition, but renal papillary necrosis and infarction are rare complications, especially in children and affecting the right kidney. In SCD patients presenting with macroscopic hematuria, clinicians must be aware of this rare condition, since prompt recognition and treatment are of high importance to reduce long-term kidney sequelae.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-276 - Chronic Kidney Disease in pediatric patients with neurogenic bladder: performance of creatinine and cystatin-based formulas

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Background: Estimation of glomerular filtration rate (eGFR) is essential for kidney function evaluation and surveillance of pediatric patients with neurogenic bladder (NB). Due to decreased muscle mass in children with NB, there may be significant inaccuracies when using creatinine-based eGFR formulas. This study aims to compare eGFR obtained by different formulas, using serum creatinine and/or serum cystatin C, in children with NB.
Methods: Data on pediatric patients with NB, with stable renal function, were collected in a Pediatric Nephrology Division from a tertiary hospital. eGFR was calculated using CKiD-Cr(Schwartz bedside), CKiD-CysC, Zappitelli-CysC, Schwartz combined-Cr/CysC and Zappitelli combined-Cr/CysC formulas.
Results: Thirty-four patients were included, 52.9%(n=18) were male, with a median(25^{th}-75^{th}percentile) age of 12,87 years(8.94-16.85). Myelomeningocele was the most common etiology(65%). In the whole sample, medians(25^{th}-75^{th}percentile) eGFR were calculated with several formulas: CKiD-Cr 99.6(61.4-129), CKiD-CysC 71.7(49.5-93.6), Zappitelli-CysC 77.1(51.7-102.7) Schwartz combined-Cr/CysC 80.9(52.2-104.4) and Zappitelli combined-Cr/CysC 91.9(56.6-123.9)mL/min/1.73m^2. Cystatin C (CKiD-CysC and Zappitelli-CysC) based formulas yielded significantly lower estimations compared to the creatinine-based Schwartz bedside formula($p<0.05$ for both comparisons). eGFR calculated with CKiD-CysC formula were significantly lower than eGFR calculated with the Schwartz combined-Cr/CysC and the Zappitelli combined-Cr/CysC formulas ($p<0.05$ for both comparisons). The eGFR calculated with Zappitelli-CysC formula was lower than the eGFR calculated with Zappitelli combined-Cr/CysC($p<0.05$). When the CKiD-CysC equation was used for GFR estimation, the CKD classification was changed, with 14 patients(41.2%) moving to a more advanced CKD stage.
Conclusion: In pediatric patients with decreased muscle mass, creatinine based eGFR formulas have several limitations. For this reason, specifically in NB patients, it is important to study alternative GFR estimations and cystatin C-based might be more sensitive for CKD staging. Further studies are needed, namely with comparison to exogenous methods of GFR determination, but cystatin C might be a valuable and more sensitive marker in this specific setting of patients with high risk for CKD progression.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-277 - Chronic Kidney Disease and Renal Outcomes Following Pediatric Heart Transplant

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Background: Children undergoing heart transplantation are at increased risk for the development of acute kidney injury (AKI) and chronic kidney disease (CKD). We aimed to evaluate incidence of CKD (stage 1-5) in this pediatric population, as well as renal transplantation and associated mortality following heart transplantation.
Methods: A retrospective observational study of 232 heart transplant patients, from infancy to age 18 years, in the period 1/2009-1/2020 was performed with three year follow up. KDIGO AKI and CKD grading criteria were used. Patients with an initial AKI episode were analyzed at 90 days, 1 year and 3 years from the time of AKI, respectively. The eGFR at the 90-day time point post AKI episode was termed RRI (Residual Renal Insufficiency). If eGFR satisfied KDIGO CKD staging, longitudinal analysis was done to calculate incidence of CKD at 1 and 3 years. Time to event analysis was done to assess the mortality associated with RRI.
Results: The overall incidence of AKI was 43.1%. Of the AKI subgroup 66% met our criteria for RRI at 3 months. Incidence of CKD was 69.6 %,75.9% at 1 and 3 year. 40% of the patients needing Continuous renal replacement therapy (CRRT) pre-heart transplant also needed CRRT post-transplant as well. Mean follow up after transplant was 5.2 years. Associated mortality was 16%. CRRT (p value <0.010) and Extra Corporeal Membrane Oxygenation (ECMO) (p value <0.010) in the immediate post heart transplant period (<1 month) was associated with increased mortality. 60% of the patients died while on CRRT. With the study period, 3% of patients needed a kidney transplant post heart transplantation.
Conclusion(s): Estimating RRI may aid in evaluating those children at risk for CKD at 1 and 3 years post heart transplant. Close monitoring of such patients may help in decreasing the incidence of CKD. Mortality increases with CRRT/ECMO in immediate post heart transplant period.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-278 - Predictive factors in Fontan associated nephropathy

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Introduction: Fontan's operation is the current surgical procedure for the treatment of congenital heart disease of the single ventricle, pathophysiology of its long term systemic complications are still not well understood.
Materials and Methods: We investigate the long term nephrological outcomes and possible predictive factors of chronic kidney disease in Fontan patients between 1993 and 2016 at Padua. We excluded patients with congenital renal anomalies, cardiac transplantation and redo-Fontan. All patients underwent clinical evaluation, laboratory exams with renal function, kidney ultrasound and complete cardiac evaluation.
Results: We enrolled 35 patients, 46% female and 54% male. Medium age was 17 y.o.,(range 10-31). Medium time from Fontan completion was 160 months (57-340 months). Ten patients had a functional single left ventricle(FSLV 28,5%); 21 a functional single right ventricle(FSRV 60%); 4 an undetermined single ventricle. Data from renal function assessment showed 26% of patients with stage 2 CKD. Most of them were FSRV (89%). None had laboratory markers of acute tubular damage, but 4 patients had signs of chronic tubular dysfunction

with elevation of beta 2 microglobulin (13%), 6% of patients showed reduced phosphate tubular reabsorption. Renal ultrasound showed reduced cortico-medullary differentiation in 5 patients (15%). Renal cysts were present in 2pts, nephrocalcinosis was reported in 2pts. Mean renal resistance index (IR) was pathological in 44%pts. The association between eGFR or microalbuminuria and IR was not statistically significant.
A statistical relationship between diastolic parameters and tubular damage is found (Pearson's R 0,4 and 0,48, respectively, p<0,05). Diastolic function appeared to be associated also with glomerular filtration, with direct correlation between diastolic pulmonary wave deceleration time and creatinine value (Pearson's R 0,49, p<0,05).
Conclusion: Fontan related nephropathy is associated with worsening diastolic function, which was more represented in FSRV patients. Those data suggest renal function should be closely monitored in patients with impaired diastolic function.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-280 - Circulating endothelial cells and endothelial dysfunction in children and adolescents with CKD

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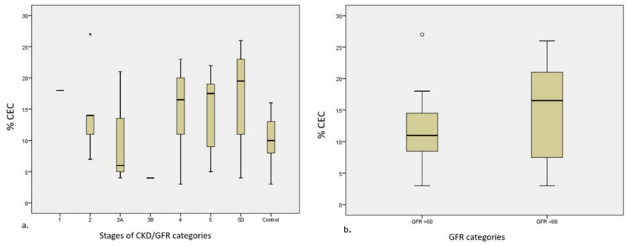
Purpose: Circulating endothelial cells (CECs) originate from the blood vessel wall and dysfunctional endothelium is a key event in the onset of atherosclerosis. Unlike biochemical indicators, CECs originate directly from the endothelium and are hence a better marker of its dysfunction. The present study intended to study the role of CEC in children including those in the early stages of CKD.
Aims and Objectives: The primary objective was to determine the correlation between the CECs to various stages of pediatric CKD. We also examined the relationship between CEC, MBD, and presence of subclinical endothelial dysfunction and atherosclerosis measured using non-invasive markers such as cIMT and Brachial FMD
Methods: 30 children with CKD were enrolled along with 15 controls. Samples were collected for measurement of circulating endothelial cells and other biochemical analyses (PTH, Vitamin D, Haemoglobin, Calcium Phosphate, CRP, and lipid profile). The carotid IMT and brachial FMD were measured. Flow cytometry (CD146+/CD144+) was used to measure CECs.
Results: The CEC's were higher in children with CKD, {mean 14.67+/-7.17 % vs 10.54+/-3.69 %, p= 0.048} with positive correlation between Stage of CKD and CEC numbers [p=0.026]. CECs also correlated with PTH [p=0.038]. No direct significant relation was found between CEC and carotid intima-media thickness and flow-mediated dilatation in various stages of CKD. Low haemoglobin levels related to higher CEC's [p= 0.033].High hemoglobin (>11.2) and an increase in serum iron were related to increased CIMT (>0.4 mm). [AUC-0.77]. Box plot in figure shows rising CEC with stage of CKD
Conclusions: The circulating endothelial cells are a useful marker for the measurement of endothelial injury and dysfunction in different stages of CKD. It is directly linked to low hemoglobin levels which may contribute to endothelial dysfunction.

Presented at: Annual Conference of the Indian Society of Pediatric Nephrology 2022



Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-281 - Functional pseudo-tumors versus malignancy in scarred kidneys. Our Experience.

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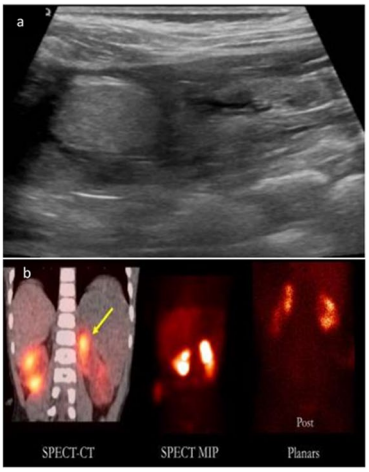
Tumor-like masses might be picked up during routine renal imaging of asymptomatic patients with chronic kidney disease (CKD). The differential diagnosis of such masses include pathological causes such as focal pyelonephritis, malignancy and granulomas, and non-pathological causes such as hypertrophied column of Bertin, persistent fetal lobulation, dromedary humps and renal regeneration nodules. The terms "renal regenerating nodule" and "nodular compensatory hypertrophy" are used in the literature to describe functioning pseudo-tumors (FPT) in the setting of an extensively scarred kidney. Differentiating these FPTs from pathological masses; especially renal neoplasms; is critical but can be challenging in the setting of CKD given the limitations related to using contrast-based imaging. Dimercaptosuccinic acid (DMSA) scan uses a non-nephrotoxic radiotracer that is picked up by functioning renal nephrons, thus offers a plausible methodology to diagnose FPTs. On DMSA scans, FPTs have a relatively normal to increased radiopharmaceutical uptake, while neoplasms (and other pathological conditions) will display an area of decreased or absent uptake. Single photon emission computed tomography (SPECT) can be coupled with DMSA to provide 3D reconstructions of the imaged kidney, leading to definite localization of the suspected lesion especially in the setting of abnormal kidney morphology. This 3D technique can be used with hybrid imaging techniques such as SPECT-CT and SPECT-MR techniques to significantly improve specificity. We report our experience with this technique in pediatric patients with CKD and history of urinary tract infections, in which tumor-like lesions evolved in scarred kidneys and were incidentally discovered on routine renal imaging. The masses showed radiotracer uptake on DMSA scans thus were diagnosed as

FPTs. Follow-up imaging showed stable size and appearance of the masses and favored a benign etiology.



US and DMSA planar and SPECT images of one of our 5 CKD patients. This patient is a two-year-old boy with a known history of posterior urethral valve status post valve ablation and bilateral ureterostomies with subsequent development of CKD stage 4 and a history of recurrent UTIs. A routine US (Figure A) that was done for the evaluation of the pelvi-calyceal system prior to ureterostomy closure showed an incidental finding of a left upper pole echogenic renal mass that was not reported on previous US. Parents denied history of increased irritability, change in urine smell or color and particularly no hematuria. Physical exam showed an afebrile, thriving, normotensive boy and no abdominal masses. To evaluate the mass, a two-dimensional (2D) planar DMSA scan was done as well as three-dimensional (3D) SPECT imaging of the kidneys (Figure B). The mass is best seen on 3D SPECT-CT and SPECT-MIP images compared to planar images showing radiotracer uptake and found to be a FPT. Its size was static on subsequent follow up US studies 18 months later. No further interventions were required.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-284 - Urinary markers of kidney injury in children with type 1 diabetes mellitus

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Background: The search for new early markers of kidney injury in children with type 1 diabetes mellitus (DM1) is fundamentally important for preventing the development and progression of chronic kidney disease.
Purpose of the study: To determine the diagnostic value of new urinary markers of kidney injury in children with DM1.
Patients and methods: Total 71 children with type 1 diabetes were examined, mean age was 12.3±3.2 years. The levels of KIM-1/Ucr, β2-m/Ucr, NGAL/Ucr and IL-18/Ucr in urine were determined. Diseases of the kidneys and urinary tract were excluded in all children. The control group included 50 apparently healthy children with the same average age. Statistical analysis was carried out using the program STATISTICA 6.0 according to generally accepted methods of variation statistics.
Results: KIM-1/Ucr was significantly higher in children with DM1 compared with the control group: 351.67pg/mg [179.28; 566.43] and 135.99pg/mg [60.03; 248.75], p=0.0000001, as well as IL-18/Ucr: 0.05ng/mg [0.04; 0,08] and 0.04ng/mg [0.03; 0.05], p<0.04. The level of β2-m/Ucr and NGAL/Ucr in patients did not differ from the healthy children: for NGAL/Ucr- 0.32ng/mg [0.12; 1.20] and 0.17ng/mg [0.03; 0.79], for β2-m/Ucr- 3.39mcg/mg [0.78; 4.82] and 4.63mcg/mg [1.75; 9.73]. We have been studied these markers according to duration of DM1: up to 6 months, from 6 to 36 months, from 36 to 60 months and >60 months of the disease. There were no differences between the level of all urinary markers in the indicated above periods of disease.
Conclusion: Urinary KIM-1 and IL-18 may have diagnostic value for functional changes in the tubular system of the kidneys in children with DM1.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-285 - Headache, Blindness and Retinal Detachment as the only pointer to End Stage Kidney Disease in a 15 year old girl: A case report.

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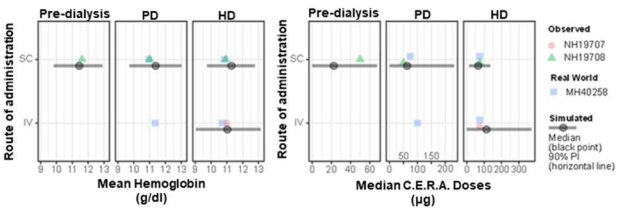
Abstract: Chronic kidney disease (CKD) among children is on the rise, both locally and globally. The burden of managing CKD in children from resource-poor centres and the developing nations as a whole, is quite challenging. Paediatric CKD has remained a death sentence in many poor nations of the world, Nigeria inclusive. This, therefore, re-emphasizes the need for nephro-prevention in children, and a higher index of suspicion for CKD, with the intention of reducing or halting disease progression at earlier stages of the disease.
CKD is asymptomatic in its earliest stages (stage I and stage II), although urinalysis findings or blood pressure may be abnormal. As chronic kidney disease progresses to more advanced stages, signs and symptoms greatly increase, making the diagnosis of CKD more obvious.
We hereby report a rare presentation of only headache, sudden blindness and retinal detachment in a 15 year old girl with end stage kidney disease (ESKD).

Keywords: CKD, Children, Headache, Blindness, ESKD, Case-report.

	IPPN (2007–Q2 2021) n = 177	IPHN (2013–Q2 2021) n = 52
Male, n (%)	110 (62%)	32 (62%)
Median age†, years (IQR)	10.6 (4.2,14.6)	14.1 (10.4,16.2)
Median body weight†, kg (IQR)	26.6 (13.9,39.2)	40.0 (27.1,55.0)
C.E.R.A. Route of administration, n (%)†		
IV	46 (26%)	49 (94%)
SC	75 (42%)	3 (6%)
Unknown	56 (32%)	0
Median observation time under CERA††, months (IQR)	6.1 (0,12.5)	11.9 (0,17.9)
Median monthly dose, µg (IQR) ‡	100 (50,150)	80 (54,129)
Median monthly dose, µg/kg (IQR) ‡	3.5 (2.3,5.1)	2.1 (1.2,3.4)
Median monthly dose, µg/m² (IQR) ‡	95 (62,145)	63 (40,98)
Mean hemoglobin levels, g/dL (SD)‡	10.9 (1.7)	10.4 (1.7)
Patients with hemoglobin within 10–12 g/dL, n (%)‡	83 (47%)	25 (48%)
Observed annualized hospitalization rates ¶	68%	69%



†At first observation.

††Estimation as true duration is not known.

‡At last observation.

¶Based on median observation times of 13.5 months and 18.3 months of patients in IPPN and IPHN, respectively. The most common causes of reported hospitalizations were due to non-elective PD/HD technique complications, infections, and cardiovascular, fluid and electrolyte complications.

IQR, interquartile range; SD, standard deviation.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-286 - Differential growth in renal parenchyma compartments between pre-term and full-term children at five years old

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Background: There is a significant correlation between kidney volume and kidney length Z-scores. In preterm children, cortex growths are higher than medulla in kidney development. Studies have reported that kidney cortex-medulla relation and cortex-parenchyma relation were higher in preterm children than in full-term children at one month old, 6-months-old, and one year old (1). Our study aims to compare kidney parenchyma, cortex, and medulla growth between pre-term children and full-term children at five years old.
Methods: Prospective cohort study. Five-year-old children with a prematurity history and full-term five-year-old children were compared. Kidney parenchyma, cortex, and medulla length were measured by a radiologist. All data were presented in medians and interquartile ranges according to their non-parametric distribution. The comparisons were made through the Mann-Whitney test.
Results: 39 preterm and 17 full-term five-years-old children were included. Parenchyma thickness in preterm children was significantly lower than in full-term children (p=0.055). Nevertheless, the cortex/parenchyma ratio was significantly higher in preterm children than in full-term children (p=0.055). No significant difference was found in cortex and medulla thickness, medulla/cortex ratio, and medulla/parenchyma ratio among the groups.
Conclusion: At five years old, preterm children have significantly lower parenchyma thickness and higher cortex/parenchyma ratio compared with full-term children. Studies with higher sample size and in other regions need to be conducted for comparison.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-287 - B-cell activating factor (BAFF) and its receptors' expression in pediatric nephrotic syndrome is associated with worse prognosis

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Aim: Immune pathogenesis of nephrotic syndrome (NS) is not completely understood. We aimed to evaluate the expression of B-cell activating factor (BAFF) and its receptors in renal samples from pediatric NS patients and its relationship with renal function survival.
Methods: We conducted an ambispective study on 36 patients with pediatric NS. Immunohistochemistry for BAFF, TACI, BCMA, and BR3 was performed. Markers were evaluated on podocytes and interstitial inflammatory infiltrates (III). We performed Kaplan-Meier curves to describe renal function survival according to markers' expression.
Results: Thirty-six NS patients were included. Minimal change disease was seen in 21 (58.3%) patients, and focal segmental glomerulosclerosis in 15 (41.7%). BAFF was found in podocytes (19% of samples) and III (38% of samples), BAFF-R in one sample, TACI in 4 (podocytes and III), and BCMA in 5 samples of podocytes and 8 of III. BAFF on podocytes and III was associated with worst renal function at follow-up; those patients had a 20% probability of having GFR >90 mL/min/1.73m^2, versus 79.6% when absent **(p=0.0014)**. Patients with BAFF in III had a 38.2% probability of having GFR>90 mL/min/1.73 m^2, versus 86.7% when absent **(p=0.0049).**
Conclusion: BAFF expression in renal biopsies could be a prognostic factor for renal function.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-288 - Characterization of tertiary lymphoid structures in a phosphate-induced renal injury mouse model

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Objectives: Tertiary lymphoid structures (TLS) are immune cell aggregates found in several non-lymphoid organs, such as the kidneys, and are associated with chronic inflammation. Similar to secondary lymphoid organs, TLS can initiate an adaptive immune reaction, but their origin is not well understood. The most mature TLS stage involves a germinal center consisting of B cells surrounded by T cells, the presence of plasma cells and follicular dendritic cells (FDCs). Among others, TLS are described in aging kidneys and in IgA nephropathy. Here, we introduce high dietary phosphate load as a new model for the formation of TLS in murine kidneys.
Methods: C57BL/6N male mice received a 0.8% normal phosphate diet (NPD) or a 2% high phosphate diet (HPD) for six months. Renal tissue was collected for histology, flow cytometry analyses and cytokine array.
Results: Histological HE and PAS staining revealed a distinctive perivascular TLS formation in the corticomedullary junction of all kidneys from mice on HPD whereas no TLS were detected in renal tissue derived from NPD controls. Flow cytometry analysis suggested a significant increase of CD3$^+$ T cells, CD45R$^+$ B cells and F4/80$^+$ macrophages in kidneys form HPD mice compared to NPD. Histological staining identified CD3$^+$ cells as the most prominent cell type in TLS,

followed by $CD45R^+$ cells. $F4/80^+$ macrophages only accumulated in the periphery of TLS. Interestingly, $CD4^+CD3^-$ cells might function as lymphoid tissue inducer cells. Cluster of $CD138^+$ plasma cells, the presence of $CD21/35^+$ FDCs and an increase of IgG pointed to the existence of mature TLS. Furthermore, HPD-induced TLS were characterized by increased cell proliferation, apoptosis, collagen accumulation, and Cxcl13 chemokine secretion. The latter was confirmed by cytokine array.
Conclusions: Our data show that chronic high phosphate load induces *de novo* formation of fully matured perivascular TLS in kidney tissue from mice.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-289 - Clinical and biochemical profile of children presenting with Metabolic Bone Disease (MBD)

Kiran Sathe[1], Akshaya Bharathi[1], Disha Bhanushali[1], Ashwini Shirsat[1], Ankit Panchal[1], Megha Warad[1], Vaishali Tiwari[1], Dhruv Parekh[1]
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Introduction: MBD is under recognized & associated with poor quality of life. It has diverse etiologies, needs appropriate evaluation and treatment.
Aim: To study clinical presentation, biochemical profile and etiology of MBD in children
Materials:
Study design: Cross sectional observational study
Subjects: Successive children under 18 y age, presenting with clinical features of MBD to pediatric nephrology clinic in last one year.
Methods: Retrospective analysis of demographic data, clinical features, biochemical profile and etiology of children presenting with MBD done.
Results: Nineteen children; 10 boys and 9 girls were included. Mean age at presentation was 74.5 months (age range 4 weeks to 15 years); Age groups 0-2 y (5/19); 2-5y (6/19); 5-18 (8/19). Presenting features bony deformities (18/19); short stature (16/19); Fractures (3/19); bony pains (3/19). Anemia (9/19); dental caries (4/19); edema (2/19), tetany (2/19). Contributory family history 2/19. Biochemical profile hypocalcemia (7/19); hypercalcemia (2/19); normocalcemia (10/19); hypophosphatemia (7/19); normal phosphorus (12/19); low 25 OH Vitamin D (12/19); elevated 1,25 OH vitamin D (2/19); elevated PTH (5/19); low PTH (1/19); elevated creatinine (3/19); hypercalciuria (8/19); metabolic acidosis (12/19); nephrocalcinosis (2/19). Etiology of MBD - distal RTA (6/19); nutritional vitamin D deficiency rickets (VDR) (6/16); CKD (2/19); proximal RTA (2/19); hypophosphatemic rickets (1/19); Vitamin D dependent rickets type 2 (1/19): osteogenesis imperfecta XI (1/19), fibrous dysplasia (1/19). Scurvy 2/19 cases. Treatment - oral alkali (9/19), bisphosphonates (2/19), vitamin C (2/19) in addition to calcium, vitamin D therapy in majority.
Conclusions: MBD was seen in all age groups secondary to diverse etiologies. Metabolic acidosis (63%)and hypercalciuria (42%) denotes tubular defect & needs attention. Nutritional anemia (31%); scurvy (10%) and VDR in 37.5% cases. Vitamin D and calcium therapy should be selectively prescribed. CKD (15%) related MBD needs consideration. Rare etiologies may present with MBD. Fractures signify severe osteoporosis and may require bisphosphonate therapy.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-290 - Validating modelling-based predictions of Continuous Erythropoietin Receptor Activator (C.E.R.A.) using real-world and clinical trial data of pediatric patients with chronic kidney disease (CKD): updated analysis from the IPDN registries

Franz Schaefer[1], Samer Mouksassi[2], Laura Benner[3], Anja Sander[3], Felix Jaminion[4], Pascal Chanu[5], Loes Rutten-Jacobs[6], Sylvie Meyer Reigner[7], Milena Studer[7], Nicolas Frey[8]
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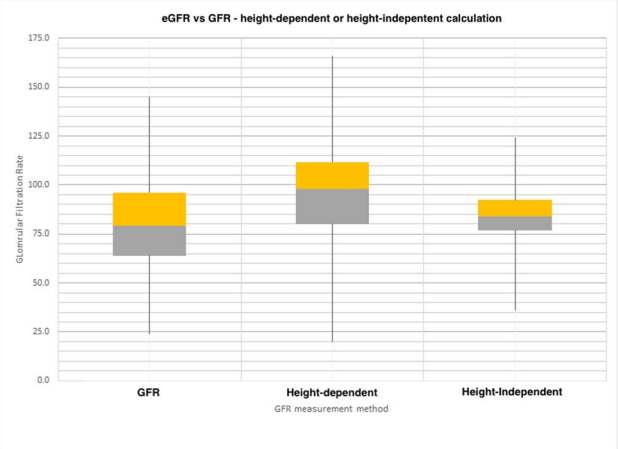
The International Pediatric Dialysis Network (IPDN, www.pedpd.org) maintains two global registries of pediatric patients on chronic peritoneal dialysis (PD) and hemodialysis (HD); IPPN and IPHN. An observational real-world study (MH40258) used these registries to assess the safety, dosing, and hemoglobin levels associated with C.E.R.A. in pediatric patients with CKD on dialysis to supplement existing trials, DOLPHIN (NH19707) and SKIPPER (NH19708) (intravenous [IV] and subcutaneous [SC] C.E.R.A. administration respectively), which established the pediatric dose conversion factor between epoetin alfa/beta or darbepoetin and C.E.R.A., and determined the safety and efficacy of C.E.R.A. for anemia maintenance treatment in pediatric patients. We compared the real-world and clinical trial data with simulations from a population pharmacokinetics/pharmacodynamics (PK/PD) model to evaluate the predictive performance of the PK/PD model.
MH40258 retrospective assessment included patient demographics, clinical characteristics, treatment, laboratory parameters, and the number and causes of hospitalization events and deaths reported; the registry performs follow-ups approximately every 6 months. The PK/PD model was developed using clinical trial data in pediatric and adult patients following IV or SC C.E.R.A. The simulations were performed in pediatric patients and compared to the longitudinal data and clinical endpoints from patients in MH40258.
The table shows analysis results of MH40258, and the figure compares simulated data to MH40258 and observed data in DOLPHIN and SKIPPER. Simulated mean hemoglobin and median C.E.R.A. SC and IV doses per dialysis modality agreed with those observed in the IPDN registry. The results confirmed the predictive performance of the PK/PD model and provided additional evidence of consistency of outcomes between clinical trials and real clinical practice. Further model-based simulations will be presented at the IPNA congress.
The IPDN registries' real-world data were consistent with the clinical data and the PK/PD model predictions on hemoglobin and C.E.R.A. dose levels, and confirm the predictive performance of the model.



Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-291 - Feasibility study into height-independent calculation and lab-reported estimation of GFR in paediatric patients

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Background: Height-dependent calculation of eGFR using the Modified Schwartz formula is the standard method of estimating eGFR from creatinine measurements. Children with undiagnosed CKD may have creatinine results within a laboratory's normal range, and rarely have eGFR calculated using height-dependent formulas. Height-independent formulas allow for auto-reporting of eGFR with laboratory results, aiding early recognition of abnormal renal function. This study compares height-dependent and height-independent eGFR calculations with concurrent formal nuclear medicine GFR results.
Methods: All paediatric patients who had a formal nuclear medicine GFR measured in a large tertiary children's hospital throughout 2018 were included in this retrospective study. Each patient had a height-dependent eGFR calculated using "Modified Schwartz formula" (eGFR = 0.36 x height/ serum creatinine) and height-independent eGFR calculated using "Nottingham-optimised Modified BCCH2" (eGFR = Inverse ln of: 6.064 + (0.554 × ln[1/ SCr(μmol/L)]) + (0.254 × ln[age]) + 0.025 if male). These results were compared with formal calculated GFR.
Results: 200 children were included, with formal GFR ranging from 25 - 147. The majority of children (120, 60%) had normal renal function (GFR >90). Of those with an abnormal GFR, height-independent formula gave a closer estimation of GFR than height-dependent formulas. Height-independent calculation was most similar to GFR when GFR 60-90.

Conclusion: Height-independent estimation of GFR gave a closer approximation to formal GFR than height-dependent calculation, especially when eGFR >60. This feasibility study suggests that laboratory auto-reporting of eGFR in children is possible and may improve early diagnosis of children with CKD.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-292 - Cardiovascular properties in children with chronic kidney disease (CKD)

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Aims: To examine whether cardiovascular properties differ according to severity of chronic kidney disease (CKD).
Methods: Data was taken from HOTKID, a multicentre UK based study which recruited children with CKD and contemporaneous controls between 2012 and 2016. All participants underwent collection of demographic and anthropometric data, haematology/biochemistry, echocardiography, measurement of blood pressure (BP) and arterial tonometry using the Sphygmocor device. Data were analysed by analysis of covariance according to eGFR <60 (group 1) vs. ³ 60 (group 2) ml/min/1.73m^2 vs. healthy controls (group 3).
Results: 100 children were included in this analysis: 22 healthy controls, 53 in group 1 and 25 in group 2. Participants had a mean age ± standard deviation (SD) of 11.3 ±3.0 years and 45% were female. Age, sex, height, weight, BP and heart rate were similar between groups. Comparison of demographic and cardiovascular properties is shown in table 1. There was no significant difference in peripheral or central blood pressure, carotid femoral pulse wave velocity (cfPWV) or left ventricular mass index (LVMI), between groups. Central augmentation index (cAIx) was higher in group 1 compared to group 3 (11.35% [±11.8] vs 1.61% [±11.5], p = 0.013). Group 1 showed a trend towards higher augmentation pressure (AP) and lower central pulse pressure (PP) amplification compared to group 3.

Table 1: demographic and haemodynamic measures stratified by eGFR

	Group 1 <60 ml/min/1.73m^2 (n=25)	Group 2 >60 ml/min/1.73m^2 (n=53)	Group 3 Controls (n=22)	P value
eGFR (ml/min/1.73 m^2) (n=100)	49.4 (±10.8)	98.8 (±22.3)	117.8 (±15.3)	**<0.001** a,b,c
Antihypertensive medication (%)	32.0	43.4	0	**<0.001**
Peripheral SBP (mm Hg) (n=100)	101.8 (±9.6)	105.1 (±12.2)	102.8 (±12.5)	0.48
Peripheral SBP z-score (n=100)	-0.12 (±0.88)	0.11 (±1.01)	-0.11 (±0.97)	0.52
LVMI (g/m^2) (n=100)	29.2 (±8.4)	29.2 (±5.3)	27.4 (±6.9)	0.53
Carotid femoral PWV (m/s) (n=100)	5.39 (±0.76)	5.64 (±0.69)	5.41 (±0.62)	0.23
Central SBP (mm Hg) (n=100)	87.0 (±9.7)	89.3 (±10.9)	86.4 (±9.1)	0.45
Central Augmentation Index (%) (n=100)	11.35 (±11.8)	4.05 (±12.3)	1.61 (±11.5)	**0.013**[b]
Augmentation Pressure (mm Hg) (n=99)	2.84 (±3.64)	1.19 (±3.63)	0.55 (±4.11)	0.088
Central PP (mm Hg) (n=99)	21.6 (±10.4)	23.3(±9.5)	23.2 (±11.0)	0.79
Central PP Amplification (n=99)	1.58 (±0.17)	1.68 (±0.18)	1.65 (±0.14)	0.07

P values reflect differences between groups following analysis of covariance (continuous variables) and chi square (categorical variables) analyses. eGFR, estimated glomerular filtration rate; LVMI, left ventricular mass index; PWV, pulse wave velocity; SBP, systolic blood pressure; PP, pulse pressure
[a] Significant difference between control and eGFR >60 ml/min/1.73m^2
[b] Significant difference between control and eGFR <60 ml/min/1.73m^2
[c] Significant difference between eGFR >60 ml/min/1.73m^2 and eGFR <60 ml/min/1.73m^2

Conclusion: In this sample including children with predominantly early stage CKD, there were no significant differences in markers of target organ damage (cfPWV and LVMI) between groups, consistent with previous published data. An eGFR <60 ml/min/1.73m^2 was associated with higher cAIx compared to healthy controls or children with eGFR ≥ 60 ml/min/1.73m^2. This suggests differing ventricular dynamics or arterial pressure wave reflection is associated with impaired eGFR in children with CKD and requires further investigation.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-293 - The Hypertension Optimal Treatment in Children with Chronic Kidney Disease (HOT-KID study): a randomised trial to compare intensive versus standard blood pressure targets on target organ damage in childhood CKD

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Background: Optimal target blood pressure to reduce cardiac damage in children with chronic kidney disease (CKD) is unknown.
Methods: Children with pre-dialysis CKD (n=124), mean eGFR 81.7 (SD 26.8) ml/min/1.73m^2, were randomised to standard treatment (auscultatory office systolic blood pressure target between the 50th-75th percentiles) and intensive treatment (systolic target <40th percentile). The primary outcome was mean annual difference in left ventricular mass index by echocardiography measured by a blinded observer, with median follow-up of 38.7 (IQR 24.1) months.
Results: Throughout follow-up, mean systolic/diastolic (SD) blood pressure in the intensive-treatment group was 103/60 (10/10) mmHg, z-score 0.06/-0.27 (0.88/1.09) and 107/64 (10/12) mmHg, z-score 0.19/0.004 (0.80/1.16) in the standard-treatment group (all P<0.001 for SBP, DBP). The average annual reduction in left ventricular mass index was similar for intensive and standard treatments: -1.9g/m$^{2.7}$ (95% confidence interval [CI] -2.45 to -1.34) versus -1.2g/m$^{2.7}$ (95% CI -1.54 to 0.82, P=0.76). However, at baseline elevated relative wall thickness was more marked than increased left ventricular mass index and a reduction in relative wall thickness was greater for the intensive compared to the standard treatment: -0.01 (95% CI -0.015 to -0.006) versus -0.004 (95% CI -0.0083 to 0.0011, P=0.002). Intensive treatment was not associated with significantly worse renal outcomes or greater adverse effects.
Conclusions: These results suggest that cardiac re-modelling in children with CKD is closely related to blood pressure control. A target office systolic blood pressure at the 50th percentile is close to the optimal target for preventing adverse cardiac remodelling.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-294 - Prostaglandin E2 (PGE2) receptors in hyperfiltration-mediated injury in solitary functioning kidney (SFK): Opposing roles for EP2 and EP4.

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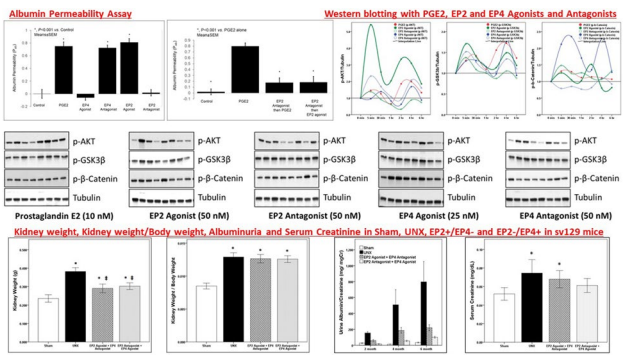
PGE_2 receptors, EP2 and EP4, are both G-protein coupled receptors. EP4 is constitutively expressed while EP2 is inducible in podocytes. Previously, we demonstrated a 1.5–2.0-fold increase in fluid flow shear stress along with increased EP2 expression and β-catenin activation in podocytes in mice with unilateral nephrectomy (UNX). Presently, specific receptor agonists and antagonists were used to evaluate the contribution of EP2 and EP4 in podocytes, glomerular filtration barrier, and kidney function in hyperfiltration-mediated injury in SFK.
Glomerular filtration barrier function was assessed by in vitro albumin permeability (P_{alb}) assay. As shown in Figure, an impaired barrier function was indicated by increase in P_{alb} induced by PGE_2, EP2 agonist (EP2+) and EP4 antagonist (EP4-), but not by EP2 antagonist (EP2-) and EP4 agonist (EP4+). Pretreatment with EP2- blocked the effect of both PGE_2 and EP2+ on P_{alb} confirming a protective effect of EP2 antagonist. Modulation EP2 and EP4 also induced opposite effects on phosphorylation of Akt and β-Catenin shown using Western blot analysis of proteins in podocyte. Next, 4 weeks old sv129 mice underwent unilateral nephrectomy and were treated with combinations EP2+/EP4- or EP2-/EP4+ for 6-months (Figure). These treatments did not impact adaptive hypertrophy (kidney weight and kidney weight/ body weight). The combination EP2-/EP4+ caused a robust decrease in albuminuria with no change in serum creatinine. There was no significant difference between sham and unilateral nephrectomy mice treated with individual agonist or antagonist of EP2 or EP4 (data not shown).



We show opposing roles of EP2 and EP4 under these conditions and protective effect of a combination of EP2 antagonist and EP4 agonist. Thus, EP2/EP4 is a potential target for mitigating hyperfiltration-mediated injury. These pre-clinical studies will lead to strategies for delaying the progression of CKD in transplant donors and children with SFK where no specific treatment(s) is available.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-295 - A multi-omics approach to understand Developmental Origin of Health and Disease (DOHaD) in chronic kidney disease and/or hypertension.

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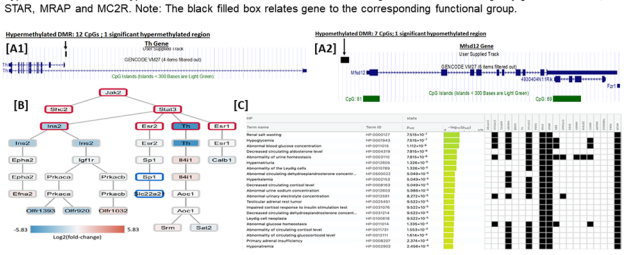
Perinatal events influence the genesis/outcome of adulthood disease (DOHaD concept). Low birthweight is associated with progression of chronic kidney disease (CKD), hypertension, albuminuria, and cardiovascular disease in adults and children. We recently described that mid-gestational IL-6 injection to pregnant mice results in offspring with low birthweight and small kidneys exhibiting accelerated maturation, activation of JAK2 and STAT3 (Sci Rep. 2021; 13260) like the inflammation observed in pregnant obese women. We applied a multi-omics approach to this model to better understand the mechanistic basis of impaired kidney development and long-term susceptibility to CKD. Pregnant mice were treated with IL-6 or saline every other day from mid-gestation. Newborn kidneys were investigated for RNA-seq, miRNA-seq and whole-genome bisulfite-seq DNA methylation profiles. EdgeR was used for differential expression analysis of mRNA and miRNA (FDR < 0.05) transcripts. Methpipe was used to determine differentially methylated CpGs (FDR < 0.05). Mixomics and G:Profiler were used for cross analysis to identify candidate targets and enriched functional groups.
IL-6 exposed kidneys showed downregulation of 65 mRNA, 18 miRNA transcripts and hypermethylation of 8,445 regions with concurrent upregulation of 38 mRNA and 27 miRNA transcripts and hypomethylation of 8,814 regions. Promoter hypermethylation and downregulation of Th (tyrosine hydroxylase) gene (Fig.[A1]) and promoter hypomethylation and upregulation of Mfsd12 (major facilitator superfamily domain containing12) gene were identified (Fig.[A2]). IMPRes algorithm revealed JAK2-STAT3 mediated downregulation of Th gene (Fig.[B]). The G:Profiler identified abnormal handling of sodium and potassium from hypoaldosteronism and hypocortisolemia as a common finding in IL-6 exposed fetal kidneys in the identified biological functional groups (Fig.[C]).

Figure: The figure shows the significant hypermethylation in the downregulated Th genes [A1] and hypomethylation site in the upregulated Mfsd12 gene [A2] in the fetal kidneys of IL-6 treated pregnant dams. [B] We had previously shown JAK2-STAT3 activation in fetal kidneys at birth following IL-6 treatment of pregnant dams (Sci Rep. 2021; 13260). After inputting the seed gene JAK2 into our in-house algorithm IMPRes v1.02, we were able to identify downstream downregulation of Th gene by STAT3. [C] G:Profiler analysis shows biological functional groups that were enriched in the fetal kidneys of IL-6 treated dams. The analysis identified abnormal handling of sodium and potassium by the renal tubules due to hypoaldosteronism and hypocortisolemia as a common theme from downregulation of the following key genes: HSD3B1, STAR, MRAP and MC2R. Note: The black filled box relates gene to the corresponding functional group.



Present multi-omics analysis of newborn kidneys exposed to maternal IL-6 suggests JAK2-STAT3 mediated Th gene downregulation and abnormality in electrolyte handling by the kidney that may play a role in future susceptibility to CKD and/or hypertension.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-296 - Diagnostic capability of new potential biomarkers in pediatric chronic kidney disease.

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Pediatric chronic kidney disease (CKD) is a clinical syndrome characterized by progressive renal function deterioration. The diagnosis is based on glomerular filtration rate (GFR), but it lacks reliability, especially at the early stages of CKD. A recent metabolic study has suggested new potential biomarkers that may help early diagnosis and better outcome. In order to verify the usefulness of these biomarkers, an extended assay has been performed on a broader cohort of CKD pediatric patients from two different countries of origin. Seventy children with CKD and fifty-three healthy children were enrolled in the study. Chromatographic analysis of blood samples was carried out on a triple quadrupole mass spectrometer (LC-QQQ), equipped with an electrospray source (ESI). The multivariate analysis showed that citrulline (CIT), n-butyrylcarnitine (nC4), and symmetric dimethylarginine (SDMA), in addition to creatinine (CNN), are useful to differentiate between control and disease populations. These biomarkers are helpful in the early stages of the disease and, regardless of its origin, improve the diagnostic reliability of the CNN itself. The multivariate *Receiver* Operating Characteristic curve including eight analytes provides an AUC of 0.730, which is higher than the AUC obtained from CNN alone. Therefore, metabolite panel assessment has more excellent utility in the diagnosis of pediatric CKD.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-297 - Coronavirus-19 infection among children enrolled in the North American Pediatric Renal Trials and Collaborative Studies registry

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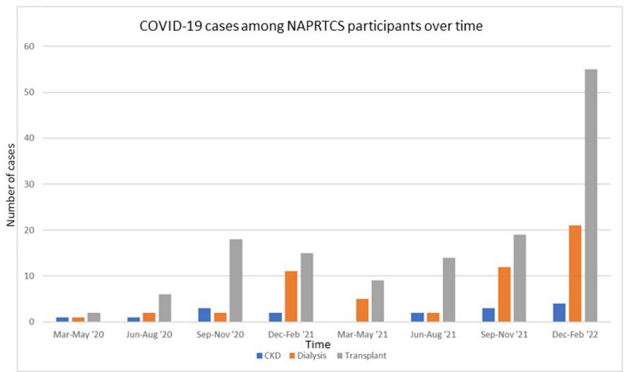
Background: Coronavirus-19 (COVID-19) disproportionately affects individuals with chronic kidney disease (CKD), however data regarding outcomes of COVID-19 infection in children with CKD are limited. We aimed to describe diagnosis, treatment, and outcomes of COVID-19

infections among children enrolled in the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) registry.
Methods: A COVID-19 specific questionnaire was added to the NAPRTCS data collection tool in October 2020 and was completed for participants with COVID-19 infection. Centers received periodic reminders to complete forms, though no specific prompt existed. Data were extracted in March 2022, and we performed a descriptive analysis for this study.
Results: Forms were submitted for 211 children from 21 centers, 16 in the CKD arm of NAPRTCS, 56 in the dialysis arm, and 139 in the transplant arm. Surges of COVID-19 infection in NAPRTCS participants followed those seen across the United States, with a spike in winter 2021, and a larger spike in winter 2022 (see Figure 1). The median age was 14.4 (8.9, 17.66), 58% of participants were male, 24% were black, 55% were white, and 15 % were 'other' race; 31% were Hispanic. 73% of participants were symptomatic, and the most common symptoms were cough (47%), fever (40%), and malaise (33%). Hospitalizations occurred in 12.5% of children in the CKD arm, 30% in the dialysis arm, and 25% in the transplant arm. Among hospitalized transplant patients, 14% developed AKI, and 34% required respiratory support. 59% of hospitalized dialysis patients needed respiratory support. There were 5 cases of Multisystem Inflammatory Syndrome in Children in our sample, and no deaths reported.
Conclusions: Among the cases of COVID-19 infection in children with kidney disease, 25% overall required hospitalization, with complications including AKI and need for respiratory support. Ongoing study of the long-term impacts of COVID-19 infection in children with CKD is warranted.

Figure 1



Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-298 - Septal diastolic alterations are highly prevalent and associated with markers of myocardial fibrosis in cardiac MRI

Tim Alexander Ubenauf[1], Jeannine von der Born[1], Carl Robert Grabitz[1], Nima Memaran Dadgar[1], Rizky Indrameikha Sugianto[1], Nele Kanzelmeyer[1], Bernhard Magnus Wilhelm Schmidt[2], Jan Falk[3], Diane Renz[3], Anette Melk[1]
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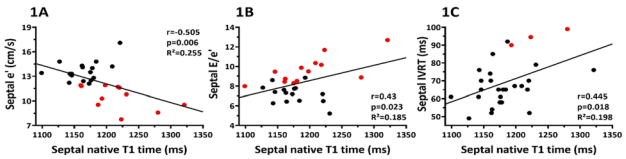
Introduction: Diastolic dysfunction in chronic kidney disease (CKD) patients often persists after kidney transplantation (KTx). Myocardial fibrosis is considered to cause diastolic dysfunction, which is an independent predictor of mortality in these patients. Native myocardial T1 relaxation time (nT1) in cardiac MRI has a high sensitivity in early detecting myocardial fibrosis. Our aim was to assess left ventricular (LV) diastolic parameters and nT1 in pediatric KTx-recipients allowing for an early identification of high risk patients.
Methods: 28 KTx-recipients (50% male; age 15.9±3.1 years) were examined. Echocardiographic parameters for diastolic function included: E-/A-wave, E/A-ratio, e´, E/e´-ratio, IVRT. Cardiac MRI (Siemens Vida 3T Scanner) was used to assess septal/mitral nT1. Pearson correlations were used to test for significances. We are currently investigating healthy controls (one control per patient).
Results: The prevalence of increased LV stiffness was high (39% had reduced septal e´-values, 14% reduced mitral e´-values) and alterations of LV compliance (i.e. increased E/e´-ratio at septal/mitral annulus) were found in 46% respectively 29%. Significant correlations with septal nT1 were seen for septal e´ (r=-0.505; p=0.006; **Fig. 1A**), septal E/e´-ratio (r=0.43; p=0.023; **Fig. 1B**) and septal IVRT (r=0.445; p=0.018; **Fig. 1C**). Comparing KTx-recipients with normal diastolic function with those having two or more diastolic parameters out of normal range, septal nT1 was significant longer in patients with diastolic abnormalities (p=0.0472).



Red dots indicate patients where echocardiographic parameters are increased/decreased.

Conclusion: We report on the under-recognized but highly prevalent clinical problem of subclinical altered diastolic function in pediatric KTx-recipients. Our demonstration of a close correlation of septal LV diastolic function parameters and nT1 indicative of myocardial fibrosis should lead to the consideration of cardiac MRI more frequently. Early detection of high risk patients is of key importance for preventing major cardiac events.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-299 - Predictors of diminished cardiac function in Filipino pediatric patients with chronic kidney disease V: A retrospective cross-sectional study

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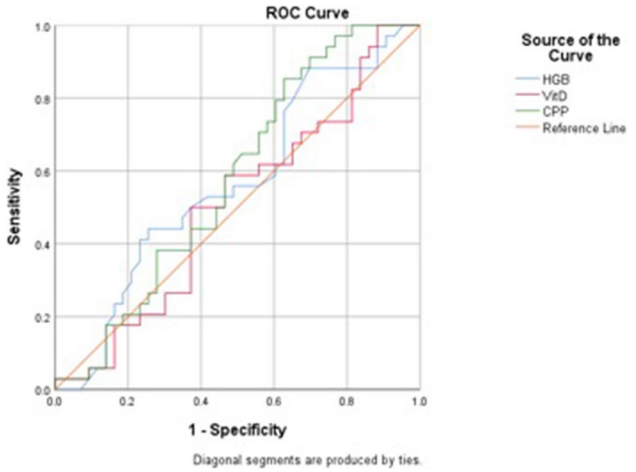
Introduction: End-stage renal disease - associated cardiac morbidity significantly contributes to a decreased life expectancy among pediatric patients with chronic kidney disease (CKD). The prevalence of systolic and diastolic dysfunction increases in patients on maintenance dialysis. Efforts have been made to determine the predictive laboratory tests appropriate to improve patient survival.
Objective: The aim of the study was to determine the predictors of diminished cardiac function in pediatric patients with CKD stage V in a tertiary subspecialty center in the Philippines.
Methodology: This was a retrospective cross-sectional study, which included a total of 77 pediatric CKD patients on maintenance dialysis, through chart review from January 2019 to December 2020 at the National Kidney and Transplant Institute.

Results: The potential of vitamin D, calcium-phosphorus product, hypertension, and hemoglobin levels to predict left ventricular dysfunction, exhibited by a decreased ejection fraction, was studied using linear regression. All of the parameters showed no relationship, except for the calcium-phosphorus product. Receiver operator characteristic (ROC) curve showed that the hemoglobin area under the curve (AUC) was 0.565 with a P value of 0.330 and a cut off value of 9.6 g/dl with 88% sensitivity and 31% specificity. The cut-off value of 18.8 ng/dl was found to be 70.6% sensitive and 33% specific in the Vitamin D ROC curve. Calcium-phosphorus product showed an AUC of 0.579 with a P value of 0.236 and a cut-off value of 65.91 with a sensitivity of 91.2% and a specificity of 31%.



Conclusion: This study showed that Vitamin D, hemoglobin and hypertension are not good predictors of cardiac dysfunction among pediatric CKD patients on maintenance dialysis. Although a statistically significant correlation was noted on the calcium-phosphorus product and cardiac dysfunction, it was low.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-300 - The impact of central blood pressure on cardiovascular target organ damage in pediatric kidney transplant recipients

Jeannine Von Der Born[1], Anne-Sophie Greiner[1], Lena Kohlmeier[1], Carl Robert Grabitz[1], Nima Memaran[1], Rizky Indrameikha Sugianto[1], Bernhard Wilhelm Magnus Schmidt[2], Nele Kanzelmeyer[1], Kerstin Fröde[1], Anette Melk[1]
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Introduction: Cardiovascular (CV) complications are an important cause for morbidity and mortality after kidney transplantation (KTx). In adults central blood pressure (cBP) is a better predictor of CV target organ damage than peripheral blood pressure (pBP). Data for children, especially after KTx, is scarce. Our aim was to assess the predictive power of cBP over pBP for CV damage.
Methods: Systolic (SBP) and diastolic (DBP) blood pressure were assessed in 48 KTx-recipients (age 13.0±4.2 years; 54% male; time since last KTx 5.5 ± 4.6). cBP was measured using the oscillometric Mobil-O-Graph device. Left ventricular mass index (LVMI) and pulse wave velocity (PWV) were considered as surrogate parameters for CV target organ damage. We used multivariable linear regression models adjusted for sex, age, renal function (eGFR) to compare cBP and pBP for their predictive value.
Results: 10% displayed elevated pSBP, while 36% showed elevated cSBP (>95th percentile), 23% had left ventricular hypertrophy, 37% an accelerated PWV (>95th percentile) (Fig. 1A). We found that only cSBP (but not pSBP) was a significant and independent predictor for LVMI (ß=0.359, p=0.0343) (Fig. 1B, upper panel). The introduction of cSBP to the model resulted in an overall superior model fit (R^2=0.191). While cDBP and pDBP were both predictors of PWV, cDBP displayed a higher estimate (ß=0.036) and resulted in a slightly better model fit (R^2= 0.478 vs. 0.446, Fig. 1B, lower panel).
Conclusion: In our small cohort with high CV burden, cBP was superior over pBP in predicting LVMI and PWV, both important parameters reflecting CV target organ damage. Further investigations with larger patient numbers and longitudinal assessments are surely needed. In light of the easy-to-use cBP devices, the implementation of routine cBP measurements into clinical practice would be feasible.

Fig. 1A

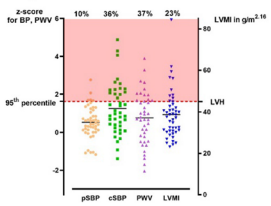

Fig. 1B

	Parameters	β	SE	p-value	Parameters	β	SE	p-value
LVMI	Intercept	9.752	21.918	0.6587	Intercept	-1.142	19.943	0.9546
	Sex	1.018	3.724	0.7860	Sex	3.522	4.087	0.3939
	Age	0.323	0.452	0.4786	Age	0.036	0.466	0.9388
	eGFR	-0.141	0.075	0.0666	eGFR	-0.140	0.073	0.0613
	pSBP	0.274	0.193	0.1621	cSBP	0.359	0.164	0.0343
	Model R^2 0.143				Model R^2 0.191			
PWV	Intercept	3.334	0.7304	<0.001	Intercept	2.867	0.818	0.0012
	Sex	-0.257	0.194	0.1920	Sex	-0.366	0.185	0.0552
	Age	0.074	0.021	0.0009	Age	0.051	0.023	0.0323
	eGFR	-0.002	0.004	0.6077	eGFR	-0.0001	0.004	0.7946
	pDBP	0.026	0.009	0.0055	cDBP	0.036	0.012	0.0029
	Model R^2 0.4463				Model R^2 0.4780			

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-301 - High impact of physical activity on cardiovascular risk factors and target organ damage in pediatric kidney transplantation recipients

Jeannine Von Der Born[1], Lena Kohlmeier[1], Anne-Sophie Greiner[1], Carl Robert Grabitz[1], Nima Memaran[1], Rizky Indrameikha Sugianto[1], Bernhard Wilhelm Magnus Schmidt[2], Kerstin Fröde[1], Anette Melk[1]

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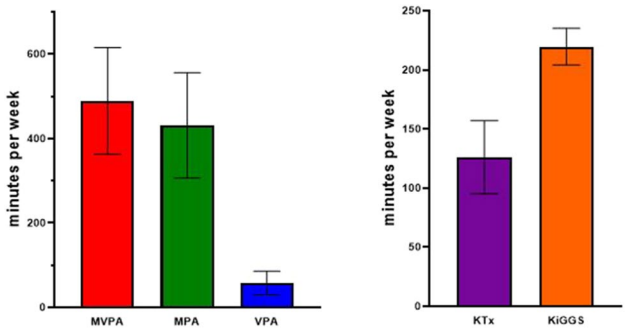
Cardiovascular (CV) morbidity is a common problem after kidney transplantation (KTx) and limits long-term survival. A high burden of CV comorbidity in pediatric KTx-recipients was previously shown. Physical activity (PA) entails CV health benefits, but information on its effect in pediatric KTx-recipients remains scarce.
48 KTx-recipients (54% male, age 13.5±4.2 years) were included. We assessed blood pressure (BP), components of metabolic syndrome, aortic pulse wave velocity (PWV), left ventricular (LV) mass index, and diastolic function. A validated PA questionnaire was used to assess minutes of moderate to vigorous physical activity (MVPA) per week, allowing to distinguish between moderate (MPA) and vigorous (VPA) intensity of activities. In a sub-cohort mean steps per day were measured using accelerometers. Linear mixed models were used to determine potential effects of PA on CV risk factors and subclinical CV organ damage.

KTx-recipients spent an average of 489 minutes per week on MVPA (Fig.1a), thereby 52% of our cohort did not fulfil the WHO recommendation of 60 minutes per week. Importantly, 54% of KTx-recipients did no VPA at all. Compared to healthy children from the KiGGS study, pediatric KTx recipients engaged in approximately half of the sporting activities (Fig.1b).

Higher MVPA levels were associated with fewer components of the metabolic syndrome (ß=-0.001; p=0.045) and were predictive of favorable parameters describing LV diastolic function such as lower A-wave velocities (ß=-0.010, p=0.021) and a better LV compliance (E/e'-ratio; ß=-0.001, p=0.008). VPA was associated with lower systolic BP z-score (ß=-0.003, p=0.025) and lower resting heart rate (ß=-0.053, p=0.006).



PA had a highly beneficial impact on CV risk factors in our small cohort of KTx-recipients. At the same time,our data reveals a relevant lack of PA (especially VPA) in these patientsLong-term CV protection through PA is could be promising in pediatric KTx recipients and should therefore be further investigated in clinical trials.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-304 - Ascertaining the optimum starting dose of subcutaneous (SC) C.E.R.A. for maintenance treatment of anemia in pediatric patients with chronic kidney disease (CKD) on dialysis or not yet on dialysis

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Background: While previously determined for intravenous (IV) administration, the optimum starting dose of subcutaneous (SC) continuous erythropoietin receptor activator (C.E.R.A.) for the maintenance treatment of anemia in pediatric patients with CKD on or not yet on dialysis requires further study.
Methods: Forty patients aged 0.4–17.7 years switched from maintenance erythropoiesis-stimulating agents (ESAs) to C.E.R.A. SC, with starting doses based on conversion factors established in a previous pediatric study of C.E.R.A. IV (DOLPHIN). After a 16-week dose titration and 4-week evaluation period (core period), 25 eligible patients (hemoglobin [Hb] levels within ±1 g/dL of baseline and within 10–12 g/dL) entered a 24-week safety extension. Efficacy, safety/tolerability and pharmacokinetics/pharmacodynamics of C.E.R.A. SC were assessed.
Results: The primary endpoint was met: the mean change in Hb between baseline and the evaluation period was +0.48 g/dL (Table 1). Mean Hb concentration levels were maintained within 10–12 g/dL and within ±1 g/dL of baseline throughout the entire study period. Results were consistent in key subgroups (age group, dialysis type, prior ESA treatment).
In the secondary efficacy analysis, the number of patients with mean Hb levels within 10–12 g/dL and ±1 g/dL of baseline was consistent between the core and safety extension periods (Table 1). The median C.E.R.A. SC dose decreased over time from 75 µg at Week 1 to 50 µg at Week 41. Safety was consistent with previous reports, with no new signals. There were no deaths reported. Lower mean injection pain scores with C.E.R.A. SC vs. prior ESAs were reported by patients, parents and nurses. The bioavailability of C.E.R.A. SC was higher in pediatric patients (67%) compared with adult patients (31%).
Conclusion: Pediatric patients with anemia secondary to CKD who are on or not yet on dialysis can be safely and effectively switched from maintenance ESAs to C.E.R.A. SC.

Table 1. Efficacy results	Evaluation (core) period (n = 40*)	Safety extension period (n = 25†)
Primary efficacy		
Mean change in Hb concentration between baseline and evaluation period (primary endpoint), g/dL	+0.48	N/A
90% confidence intervals	0.20–0.76	
Standard deviation, g/dL	±1.03	
Secondary efficacy		
Patients with mean Hb concentration within 10–12 g/dL, n/n (%)	24/38 (63)	13/21 (62)
Above 12 g/dL, n/n (%)	12/38 (32)	3/21 (14)
Below 10 g/dL, n/n (%)	2/38 (5)	5/21 (24)
Patients with mean Hb concentration within ±1 g/dL of baseline, n/n (%)	19/38 (50)	12/21 (57)
Above 1 g/dL of baseline, n/n (%)	15/38 (39)	3/21 (14)
Below 1 g/dL of baseline, n/n (%)	4/38 (11)	6/21 (29)

* 38/40 enrolled patients completed the core period.
† 21/25 patients who entered the safety extension completed it.
Hb, hemoglobin; N/A, not applicable.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-306 - Risk factors associated with chronic kidney disease in pediatric cancer survivors

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Background: Pediatric cancer patients are exposed to procedures and nephrotoxins during their therapy that can result in kidney damage.
Objectives: To screen for the prevalence of chronic kidney disease (CKD) in cancer survivors considered to be at risk of kidney injury and to identify risk factors associated with the development of CKD in this population.
Methods: This was a retrospective chart review that included patients who have received nephrotoxic chemotherapy, irradiation treatment

and/or had pelvic tumors and were under follow up at Nationwide Children's Hospital between 01/01/2011 and 06/30/2021. Patients with pre-existing CKD were excluded. Variables obtained included demographics, primary malignancy, nephrotoxin exposures, chemotherapy cumulative dose, radiotherapy exposure, nephrectomy, history of stage 2 or 3 acute kidney injury (AKI), last encounter's laboratory results and blood pressure measurements. Patients were considered to have developed CKD if the creatinine-based glomerular filtration rate in their last clinic visit was <90 ml/min/1.73m2.

Results: A total of 128 patients met the inclusion criteria. The median age at cancer diagnosis was 5.4 years and the median duration of follow-up was 6 years. Hematological malignancies were the underlying tumors in 51% of patients. Nineteen percent of our patients had AKI episodes during the course of their treatment. The prevalence of CKD and hypertension were 10.9% and 32% respectively. Nephrectomy, history of AKI and Ifosfamide treatment were associated with higher risk of CKD [OR=16.4 (4.08-65.45) p <0.0001, OR=3.75 (1.17-12.06) p=0.026, and OR=10.4 (3.03-35.66) p=0.0002 respectively].

Conclusion: Nephrectomy, previous stage 2 or 3 AKI episodes, and Ifosfamide treatment were associated with increased risk of CKD development in our cohort of pediatric cancer survivors. Despite the limitations of a retrospective study, our data could provide guidance for screening guidelines in pediatric cancer survivors.

Chronic Kidney Disease (including mineral metabolism & cardiovascular disease)

P2-307 - Diurnal variations of urinary biomarkers in children with chronic kidney disease

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Abstract

Background: Twenty-four-hour urine protein excretion is well established to estimate kidney function in clinical practice. Given the inconvenience of 24-hour urine collection, spot urine or short-interval timed urine can be used as a surrogate for the quantification of proteinuria. However, the impact of collection time on the levels of urinary biomarkers is not fully known. Thus, the diurnal variations of urinary biomarkers were investigated.

Methods: Hospitalized children aged 3-17 years with chronic kidney disease were enrolled, from August 2019 to November 2019. Urine samples were collected during 21:00 (bedtime)-07:00 (waking up), 07:00-12:00, 12:00-16:00, 16:00-21:00, and again during 21:00-07:00. Urinary total protein, albumin, N-acetyl-beta-D-glucosaminidase (NAG), epidermal growth factor (EGF), collagen type I alpha 1 chain (COL1A1), and creatinine were measured for each time interval and compared with urinary specimens of 24 hours, respectively.

Results: Twenty children (14 boys, 6 girls) were enrolled, with an average age of 11.3 years. For the levels of urinary protein:creatinine ratio (PCR), albumin:creatinine ratio (ACR), NAG:creatinine ratio, and COL1A1:creatinine ratio, within-day variations were significantly higher than day-to-day (two 21:00-07:00) variations. Their levels exhibited significant diurnal variations among different time intervals within 24 hours. However, no significant diurnal variation was observed in urinary EGF:creatinine ratio (EGF/Cr). Additionally, urinary EGF/Cr levels were not significantly affected by centrifugation, additives, storage temperature, or delayed processing.

Conclusions: Given that some kidney function-related urinary biomarkers exhibit diurnal variations, our study suggests that urine samples should be collected during the same time interval in clinical practice if possible. Our study also provided evidence for urinary EGF/Cr as a relatively stable biomarker that is minimally influenced by preanalytical factors, supporting its potential clinical application.

Haemodialysis and peritoneal dialysis

P2-308 - Comparing the effect of two haemodialysis modalities on some trace elements: a pilot study from a tertiary care pediatric dialysis centre

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Background: Online hemodiafiltration (OL-HDF) increases convective clearance of solutes & molecules compared to conventional hemodialysis (HD). Consequently, patients on OL-HDF may suffer from trace elements deficiency. This could lead to serious cardiovascular morbidities and shorter life span.

Subjects & Methods: We measured and compared the serum levels of Zinc (Zn), Copper (Cu), Manganese (Mn), Cadmium (Cd), and Lead (Pb) for 105 subjects; 43 on hybrid dialysis (alternating sessions of OL-HDF and HD), 22 on HD and 40 healthy controls, all are age and sex matched. Hybrid & HD groups had comparable duration and frequency of dialysis. The hybrid group represents the effect of the OL-HDF, as at the time of data collection there were not enough subjects on OL-HDF only.

Results: Compared to HD, hybrid group had statistically significant lower Mn level (7.77±1.81µg/dL, 9.5±1.87 µg/dL, p=0.002).This group also had lower Zn & Cu levels (71.81±10.75 µg/dL, 77.02±7.35 µg/dL) compared to HD (81.18±13.45 µg/dL, 85.36±11.65 µg/dL) (p=0.018, p=0.014 respectively) & controls (80.53±13.07 µg/dL, 89.6±16.96 µg/dL) (p=0.017, p<0.001 respectively). There was no significant difference in Mn level between Hybrid & control groups. No significant difference was detected between HD & controls regarding Zn & Cu levels. Pb & Cd were comparable across the 3 groups.

Conclusion & Recommendations: Our findings suggest that patients on OL-HDF are more susceptible to trace elements deficiency especially Zn, Cu, and Mn. Consequently, we recommend regular assessment of trace elements in patients on OL-HDF as a practice guideline. Further exploration of impact of dietary intake in these patients is needed. So, phase two of this work (currently underway) will utilize a longitudinal design to understand such effect in patients exclusively on OL-HDF and establish the needed recommendations.

Age, Sex, Etiology of CKD, Duration of Dialysis Treatment, Trace Elements in Different Groups

Parameters				P-Value
Age; Mean ± SD		* Hybrid (n= 43)	10.84±3.29 years	0.33
		**HD (n= 22)	11.5±2.04 years	
		Control (n= 40)	12.43±3.62 years	
Sex (Male / Female)		Hybrid (n= 43)	20 / 23	0.94
		HD (n= 22)	11 / 11	
		Control (n= 40)	20 / 20	
Etiology of CKD; n (%)		CAKUT	27 (41.5%)	
		Chronic GN	10 (15.4%)	
		Podocytopathy	7 (10.8%)	
		Ciliopathy	6 (9.2%)	
		RPGN	4 (6.2%)	
		MCKD	3 (4.6%)	
		TMA	3 (4.6%)	
		Tumor	2 (3.1%)	
		SLE	2 (3.1%)	
		Chronic TIN	1 (1.5%)	
Duration of Dialysis Treatment; Mean ± SD		Hybrid (n= 43)	2.93±1.69 years	0.978
		HD (n= 22)	2.5±1.26 years	
Trace Elements; Mean ± SD	Mn	Hybrid (n= 43)	7.77±1.81 µg/dL	0.002
		HD (n= 22)	9.5±1.87 µg/dL	
		Control (n= 40)	8.77±2.11 µg/dL	
	Zn	Hybrid (n= 43)	71.81±10.75 µg/dL	0.004
		HD (n= 22)	81.18±13.45 µg/dL	
		Control (n= 40)	80.53±13.07 µg/dL	
	Cu	Hybrid (n= 43)	77.02±7.35 µg/dL	0.000
		HD (n= 22)	85.36±11.65 µg/dL	
		Control (n= 40)	89.6±16.96 µg/dL	
	Pb	Hybrid (n= 43)	5.37±1.69 µg/dL	0.616
		HD (n= 22)	5.28±2.24 µg/dL	
		Control (n= 40)	6.2±3.48 µg/dL	
	Cd	Hybrid (n= 43)	0.67±0.38 µg/dL	0.115
		HD (n= 22)	0.58±0.23 µg/dL	
		Control (n= 40)	0.67±0.17 µg/dL	

** Hybrid: Combined OL-HDF & Conventional HD as alternating sessions*
*** HD: Conventional hemodialysis*

Haemodialysis and peritoneal dialysis

P2-310 - Comparison of inflammatory markers in children with end stage kidney disease on hemodialysis and peritoneal dialysis

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Introduction: Patients with End-Stage Kidney Disease (ESKD) and especially those on dialysis are burdened with a high inflammatory load leading to endothelial dysfunction which results in high cardiovascular morbidity and mortality. There are very few studies comparing inflammatory markers in children on peritoneal dialysis (PD) and hemodialysis (HD).
Objective: The primary objective was to compare levels of Fibroblast Growth Factor 23 (FGF23), high sensitivity C-Reactive Protein (hsCRP) and Interleukin-6 (IL-6) in children with ESKD undergoing maintenance HD and PD.
Methods: This was a cross sectional hospital based study involving children 1-18 years of age with ESKD on maintenance HD or PD for at least 3 months at SAT hospital, Government medical college, Thiruvananthapuram. The inflammatory marker levels were compared between the two groups as well as correlated with clinical and laboratory parameters.
Results: A total of 16 children were included in the study (10 on PD and 6 on HD). All the patients on PD were on continuous ambulatory PD. The mean hsCRP was 3.14±0.59 mg/L in HD group and 3.28±0.87 mg/L (p=0.515) in PD group. The mean FGF 23 was 1.81±0.37 pg/ml in HD group and 1.50±0.56 pg/ml in PD group (p=0.913). The mean IL-6 was 821.7±137.9ng/ml in HD group and 794.6±121.6 ng/ml in PD group (p=0.233). IL-6 showed positive correlation with dialysis vintage (R=0.509, p=0.044). There was positive correlation between FGF23 and IL6 levels (R=0.547, p=0.028).
Conclusion: There is no difference in inflammatory markers viz hsCRP, IL-6 and FGF-23 in children on hemodialysis compared to those on peritoneal dialysis

Haemodialysis and peritoneal dialysis

P2-311 - Improving acute peritoneal dialysis outcome with soft catheter (Cook Mac-Loc Multipurpose Drainage catheter(R)) among infants <1500g in a low resource setting

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Objective: Improve outcome of peritoneal dialysis among very low-birth weight (VLBW, birth weight <1500 gram) and extremely low-birth weight (ELBW, <1000 gram) infants.
Design: Quality improvement project.
Setting: Lower-middle-income resource setting: Network of five participating neonatal units supported by a tertiary pediatric nephrology centre in Kolkata, India.
Patients: VLBW (n=13) /ELBW (n=11) infants who underwent peritoneal dialysis (PD) for neonatal acute kidney injury.
Interventions: Infants were initially dialysed using stylet based rigid catheter (SRC) where high PD related complications were common. Subsequently from August 2018, all PD were done by soft Cook Mac-Loc Multipurpose Drainage catheter$^{(R)}$ (CMMDC).
Main outcome measures: Comparison of PD related complications including peritonitis, survival during PD, and survival to discharge from neonatal unit between PD done with SRC and CMMDC.
Results: After changing from SRC (n=10) to CMMDC (n=14), PD related complications dropped from 9 out of 10 (90%) in the SRC cohort to 7 out of 14 (50%) in the CMMDC cohort (p = 0.04) and mortality while on PD decreased from 5 out of 10 (50%) in the SRC cohort to 1 out of 14 (7%) in the CMMDC cohort (p = 0.017). Neonates undergoing PD with CMMDC were able to undergo significantly longer duration of PD with higher net ultrafiltration and better control of acidosis in comparison to those with SRC. CMMDC was costlier than the SRC; USD 60 compared to USD 14 respectively.
Conclusions: Although costlier, undertaking PD with soft catheters (CMMDC) is feasible even among ELBW/VLBW infants and yielded significantly better results in comparison to stylet based rigid catheters.

Haemodialysis and peritoneal dialysis

P2-312 - emergency hemodialysis at the pediatric nephrology unit (unp) of Yopougon university hospital

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Aim of Study: Describe the first emergency hemodialysis sessions in African pediatric settings
Method: 50 records of children with hemodialysis from January 2016 to 31 December 2020 were analyzed
Results: The sex ratio was 0.78. The average age is 8.7 years. A delay of 48 hours elapsed between the hemodialysis' emergency and its effectivness in 69.2% of cases. The indication for hemodialysis was uremic syndrome (42%), hyperkalemia (20%) and acute lung oedema (10%). Hemodialysis was done on a femoral catheter (92.9%) with inappropriate equipment in 25% of cases. Per-dialytic incidents were dominated by low blood pressure. Renal failure's etiology was undetermined (46.1%), toxic (30.8%) or malaria (23%).
Conclusion: These results will allow to optimize care

Haemodialysis and peritoneal dialysis

P2-313 - Quality of life in children on Peritoneal Dialysis

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Background: The increasing global epidemic of chronic kidney disease (CKD) and resultant end-stage renal disease (ESRD) continues to be a serious challenge for many countries. ESRD has a substantial effect on the patient's quality of life (QoL) by negatively affecting their social, financial, and psychological well-being.
Health-related quality of life (HRQoL) is an important prognostic factor in ESRD patients on peritoneal dialysis (PD) that can be assessed using a standardized tool; the Pediatric Quality of Life Inventory™ (PedsQL™) Generic Core Scales. This tool was used to assess the HRQoL in our pediatric dialysis patients.
Methodology: The study included children aged 2–14 years with ESRD on PD, recruited from our center. Data were collected using the PedsQL™ ESRD Module questionnaire.
Result: 13 Pediatric patients on PD were included in this study. We found that there is overall agreement between parents and patients score with a positive correlation (P=0.0001), as well as a positive relation between parents score and the age of the patient at the time of the questionnaire (P= 0.020); the older the child is the higher the parent scored on the questionnaire (P=0.001).
In contrast, there was no correlation between parents' or patients' score and duration of time the patient has been on PD (P=0.912, P=0.799).
Conclusion: HRQoL scores in our patients and their parents showed agreement and positive correlation, and were higher in older patients compared to the younger age group. Interestingly, there is no significant correlation between duration on dialysis and patients or parents scores.

Haemodialysis and peritoneal dialysis

P2-314 - Kt/V or bicarbonate: What is more important for growth in pediatric peritoneal dialysis patients?

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Introduction: Growth retardation is a common problem in pediatric patients with chronic kidney disease (CKD). It is unknown if the growth of children on peritoneal dialysis (PD) can be augmented by more dialysis.
Methods: We studied the effect of various peritoneal adequacy parameters on delta height standard deviation scores (SDS) and growth velocity z-scores in 53 children (27 males) on peritoneal dialysis (PD), who underwent 2 longitudinal adequacy tests at nine-month intervals. None of the patients were on growth hormone. Intraperitoneal pressure and standard KDOQI guidelines were compared to the outcome measures delta height SDS and height velocity z-scores, using univariate and multivariate tests.
Results: At the time of the second PD adequacy test, their mean age was 9.2±5.3 years; mean fill volume was 961±254mL/m^2 and median total infused dialysate volume was 5.26 L/m^2/day (range 2.03 to 15.32 L). The median total weekly Kt/V was 3.79 (range 0.9 to 9.5) and the median total creatinine clearance was 56.6 (range 7.6 to 133.48) L/week, higher than previous pediatric studies. The delta height SDS was a median of -0.12 (range -2 to +3.95)/year. The mean height velocity z-score was -1.6 ±4.0. The only relationships discovered were between the delta height SDS and age, bicarbonate, and intraperitoneal pressure; but not for Kt/V or creatinine clearance.
Discussion/Conclusion: Our findings highlight the importance of normalization of bicarbonate concentrations to improve height z-score.

Haemodialysis and peritoneal dialysis

P2-315 - Histopathological Changes of Long-Term Peritoneal Dialysis using Physiological Solutions – A Case Report and Review of the Literature

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Long-term peritoneal dialysis, especially with non-physiological solutions, is afflicted with the severe complication of encapsulating peritoneal sclerosis (EPS). Physiologic peritoneal dialysis (PD) solutions have been introduced to reduce pH trauma. Data on peritoneal biopsies in pediatrics with long-term PD using physiological solutions are scant. We report an adolescent who had been on 10-hour continuous hourly cycles using mostly 2.27% Physioneal™ for 5 years. There were two episodes of peritonitis in October 2017 (*Klebsiella oxytoca*) and May 2018 (*Klebsiella pneumoniae*), which were treated promptly. This adolescent, who lost two kidney transplants from recurrent focal and segmental glomerulosclerosis, underwent a peritoneal membrane biopsy at the time of a third PD catheter placement, 16 months after the second renal transplant. Laparoscopically, the peritoneum appeared grossly normal, but fibrosis and abundant hemosiderin deposition were noted on histology. The thickness of the peritoneum was 200-900 (mean 680) µm; normal for age 14 is 297 [IQR 229, 384] µm. The peritoneum biopsy did not show specific EPS findings, as the mesothelial cells were intact and there was a lack of fibrin exudation, neo-membrane, fibroblast proliferation, infiltration, or calcification. While the biopsy was reassuring with respect to the absence of EPS, significant histopathological changes suggest that avoiding pH trauma may not ameliorate the effects of glucose exposure in long-term PD.

Haemodialysis and peritoneal dialysis

P2-317 - Infectious metastasis with multiple foci in children with hemodialysis catheters

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Infectious metastasis with multiple foci in children with hemodialysis catheters.

Introduction: Infectious metastases in children on RRT are rare and have high morbidity and mortality. Immunodeficiencies are predisposing factors.
Clinical Case: Female, 11 years old, with Stage 5 CKD, secondary to uropathy, with 6 months of hemodialysis by transient catheter (several catheter changes) in the left subclavian vein. He presented headache, fever and general malaise for 24 hours. Laboratories: Hb 9.6, Ht 30%, WBC 16,420, N 84, L 12 Plaq 210,000, CRP 235 mg/L. Plain urine and chest X-ray normal. Administered_ Vancomycin + Ceftazidime, empirical treatment. Echocardiogram (Day 2): non-homogeneous image, 13x7 mm, irregular borders, at the mouth of the superior vena cava, protruding into the right atrium, HMCx2 and retroculture: SARM. Antibiotic therapy: Vancomycin, Gentamicin and Meropenem. Echocardiography (D9): increase in the lesions described above, occupying a large part of the right atrial cavity, emboli in transit. Surgical resolution (D11): Sternotomy for extraction of vegetations in the aortic valve + excision of a 2.5 cm pseudocyst in the right atrium + lavage and aspirate of the left pleura, with positive cultures for MRSA in the pseudocyst in the atrium, pleural fluid, aortic valve. Pathological anatomy compatible with infectious inflammatory material. D30: convulsive episode, altered sensorium, cranial CT scan: brain abscess in the parietal lobe, 20x16 mm, without neurosurgical conduct. Medical discharge after 6 weeks of antibiotic therapy. Three months after discharge, he presented with progressive heart failure, echocardiography: severe aortic valve insufficiency. Aortic valve is replaced by a mechanical valve; after which, the patient presents improvement of the symptoms.
Conclusion: Cases of infective endocarditis at the starting point of the hemodialysis catheter in pediatric patients who require surgery for vegetative resection and valve replacement are rare, it is essential to recognize complications early because they can become catastrophic.

ISPD-IPNA Joint Session

P2-318 - Peritonitis in chronic peritoneal dialysis during 24 years in a single pediatric center

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Peritoneal dialysis (PD) is a modality of kidney replacement therapy frequently used in children with chronic kidney disease. Peritonitis is the most common complication and cause of end of therapy. The aim of our study was to describe a cohort of consecutive peritonitis' episodes (PE) in the same single pediatric center during 24 years . Methods: we reviewed the files of all the patients under 18 years old who started and stayed more than 3 months on PD in our center from 1997 to 2020. We analyzed gender, age, underlying kidney disease, signs and symptoms associated to PE, type of microorganism that caused PE, treatment and outcomes. The study was approved by the local Ethics Committee.Results: 190 patients were elligible, 121 from male gender (64%), median age at PD initiation was 7.6 years-old and 43% had CAKUT. There were 315 PE presented by 126 patients (66%). The most frequent sign was cloudy efluent in 89%, abdominal pain was referred by 69% of the patients. There were 33% of Gram-positive (GP) PE, 31% Gram-negative (GN), 28% with negative culture, 6% fungal and in 2% the culture was lost or not performed. The overall incidence rate was 0.68 episodes per patient-year (from 0.32 to 1.87). Good response to treatment ocurred in 82% of the cases, 17% were transferred to hemodialysis because of the PE and 1 patient died due to mesenteric artery thrombosis. Conclusion: Most patients had at least 1 PE, there was a predominance of GP, incidence of peritonitis is high but comparable to other cohorts and has presented a great variation during the time analyzed and we are making efforts to improve it.

ISPD-IPNA Joint Session

P2-319 - Training of caregivers for pediatric chronic peritoneal dialysis: A survey of practices and impact on peritonitis

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Introduction: Patient and care-giver training is an important tool for prevention of peritonitis and peritoneal dialysis(PD) technique failure. The objective of our survey was to study the impact of training practices on the rate of peritonitis.
Methods: A survey consisting of 44 questions was distributed to 137 member centres of the International Pediatric Peritoneal Dialysis

Network(IPPN) whose peritonitis data was collected in the IPPN registry.

Results: Responses were obtained from 62/137(45%) centres from 34 countries. In 57(92%) centres, a trained pediatric PD nurse is available. Training is performed either in a combined out-patient and in-patient (23.4%) setting, or only as in-patient(25.4%). Eighteen(29%) centres use the VARK(Visual-auditory-reading-kinesthetic) tool. Home visits are conducted during training in 36(58%) centres, and remote monitoring is used in 44(71%)centres. The median duration of training is 10(7,14) days for 24(18,40) hours. Many centres(44.7%) train 2 caregivers and 15(24%) centres train children >12 years of age. A median of 4(2,5) tools were used, with written material being used exclusively in 62%. A formal assessment is conducted after training in 55(89%) centres, with skill demonstration being tested in 51(82%) centres. Take-away materials are provided in 54(87%) centres. Re-assessment is conducted regularly in 25(40%), re-training after every peritonitis in 19(38%), and sometimes in 8(16%)centres.

Of the 445 reported peritonitis episodes between 01/2019 and 12/2020 from 49(80%) centres, 227(53%) were gram positive, 117(26%) gram negative, 107(23%) culture negative and 23(5%) fungal accounting for a rate of 0.4 episodes/patient-year. None of the practices influenced the peritonitis rate. Culture negative peritonitis rate was negatively associated with GDP($p<0.05$).

Conclusion: Pediatric peritoneal dialysis training is typically performed by trained personnel and supported by formal assessments, home visits, remote monitoring and re-training. The current analysis did not reveal a significant relationship between training practices and peritonitis rate. Future analyses will evaluate the geographic differences between training components and peritonitis rate.

Haemodialysis and peritoneal dialysis

P2-320 - Acquired cystic kidney disease: A hidden complication in children on chronic hemodialysis

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Objective: To determine the frequency of acquired cystic kidney disease (ACKD) in children on chronic hemodialysis.

Material and Methods: In this single center cross sectional study, 150 children were included who were on chronic hemodialysis for six months. Ultrasound was done to see the renal cysts. Cystic changes that could not fulfill the criteria for ACKD were also noted and analyzed.

Results: Mean age was 14.5 ± 3.5 years, of these 63 (42%) were males. ACKD was detected in 53 (35%) of the patient and 18 patients (12%) had solitary cysts. The distribution of these entities was similar across all age groups. The underlying etiologies in the descending order were unknown 64 (43%), stone disease 31 (21%), each of the congenital anomalies of the kidney and urinary tract and glomerulonephritis 23 (15%) and others 9 (6%). A higher frequency of ACKD was detected in the children on renal replacement therapy for more than two years (33 out of 53 children, 63% with p-value 0.004) Figure 1.

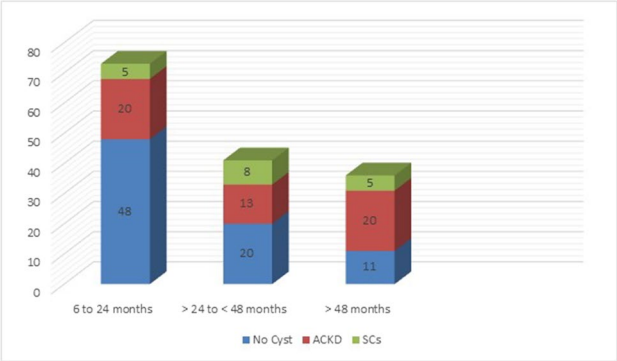

Figure 1: Association of cystic kidney diseases with duration of hemodialysis

ACKD: Acquired cystic kidney disease, SCs: Solitary Cysts

Conclusion: The ACKD was found in one third of our hemodialysis children and its frequency increases with the duration of hemodialysis. This percentage may not reflect the true prevalence as there is a lack of consensus on definition of ACKD. Periodic assessment of chronic kidney disease patients for development of ACKD especially on chronic hemodialysis is required to reduce the morbidity.

Keywords: Acquired cystic kidney disease, Solitary cysts, renal replacement therapy, end stage kidney disease, ultrasonography

Haemodialysis and peritoneal dialysis

P2-321 - Nutritional status of children undergoing chronic peritoneal dialysis in Kazakhstan: preliminary data

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Introduction: Children on chronic peritoneal dialysis (CPD) are at great risk of growth retardation and underweight. We aimed to assess the nutritional status in children on peritoneal dialysis in Kazakhstan.

Methods: We included 23 children on CPD admitted to the nephrology department. A quantitative measure of dietary intake was accomplished by conducting a prospective 3-day diet history recorded by 19 caregivers (4 records missing). Anthropometric and biochemical data were collected from medical records. In addition, we retrospectively recorded anthropometric data (height, weight) of recruited children at dialysis initiation, 6 and 12 months after. Body Mass Index (BMI) was normalized to standard deviation scores (SDS) according to WHO standards. Statistical analysis utilized ANOVA to compare differences between BMI groups and Chi2 test for assessing differences in proportions.

Results: The median age of our cohort was 7.9 (IQR 3.2 – 13.9) with boys accounted for 56.5% (n=13). Overall prevalence of underweight, normal weight and overweight/obese was 21.7%, 69.6% and

8.7% respectively. We found no statistical significance between BMI groups when comparing age, gender, renal diagnosis, height SDS, short stature, energy deficit, duration on CPD and biochemical parameters, except for c-reactive protein. Inadequate dietary energy intake was observed in 35% (n=8), including 60% of underweight and 31.25% of normal weight children. 56.5% (n=13) had short stature. Overweight patients were shorter than other BMI groups. Prevalence of underweight children of this cohort was high both at dialysis initiation and 1 year after (26.1% and 21.7% respectively).
Conclusion: Our data showed that local children undergoing CPD have high prevalence of underweight, short stature and inadequate dietary energy intake not only at dialysis initiation but also after 1 year on CPD. Further investigation of the possible underlying causes may improve nutritional management of these children

Table 1. Patient baseline characteristics.

variable	Total	BMI<-2SDS	BMI=-2 to 1.036SDS	BMI>1.036SDS	p-value
	23 (100%)	5 (21.7%)	16 (69.6%)	2 (8.7%)	
Age (yrs)	7,92 (10,75)	13,17 (9,46)	5,46 (10,46)	7,08 (-)	0,317
Male gender N (%)	13 (56.5%)	3 (60%)	8 (50%)	2 (100%)	0.399
Renal Disease:					0.735
CAKUT	9 (39.13%)	3 (60%)	5 (31.25%)	1 (50%)	
Glomerulopathy	9 (39.13%)	1 (20%)	7 (43.75%)	1 (50%)	
Other	5 (21.74%)	1 (20%)	4 (25%)	0 (0%)	
Height SDS	-2,17±1,939	-1,44±1,443	-2,15±2,049	-4,10±1,105	0,271
Ht short stature <-1.88 n(%)	13 (56.5%)	3 (60%)	8 (50%)	2 (100%)	0.399
HB g/l (mean±SD)	104,13±14,92	112,00±13,60	102,94±15,43	94 ± 7,07	0,313
WBC x 10^9/L	7,33 ± 2,91	6,98 ± 3,05	7,63 ± 3,01	5,87 ± 2,71	0,708
CRP mg/L	1,10 ± 1,46	2,33 ± 2,02	0,62 ± 0,95	1,87 ± 2,18	0,047
Serum BE mmol/L	23,34 ± 7,134	29,04 ± 11,13	21,73 ± 3,72	18,80 ± 5,80	0,093
Total protein g/L	59,91 ± 7,33	59,52 ± 8,82	60,75 ± 7,06	54,25 ± 6,86	0,515
Serum albumin g/L	36,38 ± 4,26	35,30 ± 5,65	37,11 ± 3,82	33,28 ± 4,28	0,414
Na mmol/L	132,04 ± 5,71	131,60 ± 8,33	132,19 ± 5,36	132,0 ± 2,83	0,98175
K mmol/L	4,50 ± 0,97	3,98 ± 0,60	4,60 ± 1,01	5,05 ± 1,34	0,34099
iCa mmol/L	1,08 ± 0,11	1,08 ± 0,09	1,07 ± 0,13	1,10 ± 0,04	0,96222
Phosphates mmol/L	2,01 ± 0,48	1,97 ± 0,87	2,00 ± 0,33	2,15 ± 0,62	0,90653
Energy deficit n (%)	8 (35%)	3 (60%)	5 (31.25%)	0 (0%)	0.279
Time on PD (median (IQR)	561	289 (3338)	271,5 (437)	765,5 (-)	0,15591

Haemodialysis and peritoneal dialysis

P2-322 - Barriers in nutritional management of children undergoing chronic peritoneal dialysis in Kazakhstan: parent and healthcare provider perspectives (preliminary data)

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Introduction: High prevalence of underweight (21.7%), short stature (47.8%) and inadequate dietary energy intake (35%) were observed in local pediatric patients on chronic peritoneal dialysis (CPD). We explored possible barriers in nutritional management of these children from parent and healthcare provider perspectives.
Methods: Face-to-face semi-structured in-depth interviews were conducted with parents of children on CPD admitted to the nephrology department, and with healthcare providers involved in their treatment. Transcripts were coded and thematic analysis was performed using QRS-NVivo software.
Results: Parents of 23 children on CPD and 15 healthcare professionals: 5 (33.3%) pediatric nephrologists, 8 (53.3%) renal nurses and 2 (13.3%) food distributors participated in the study. 95% of parents regarded diet as an important aspect in treatment of their children. From caregivers' interviews we identified the following themes: child-related (change of appetite, mood switch, depression and lack of independence, feeling deprived and isolated), diet related (complexity of restrictions, contradicting healthy eating, monotonous tasteless food, breaking habits), knowledge-related (focus on diet restrictions, low awareness of age-appropriate dietary intake, lack of reliable sources for self-education), healthcare system-related (trusting physician guidance and lack of self-engagement, absence of expert dietician consultation). From healthcare providers we identified the following themes: patient-related (financial insecurity, lack of understanding of diet importance and motivation, lack of family support), prioritizing acute events (physicians focused on diet restrictions that prevent development of "life-threatening" complications, low priority given to quality of diet and energy deficiency), organizational barriers (absence of multidisciplinary team with nutrition expert, inadequate staffing, limited role of nurses, lack of personalized approach and follow-up after discharge).
Conclusion: Parents' heavy reliance on physician guidance as the only reliable source of information, and the latter's prioritization of dietary restrictions alone, can be detrimental to child nutritional status. Multidisciplinary team approach with governmental support is crucial in nutritional management.

Haemodialysis and peritoneal dialysis

P2-323 - The clinical utility of reticulocyte hemoglobin concentration in pediatric chronic dialysis patients

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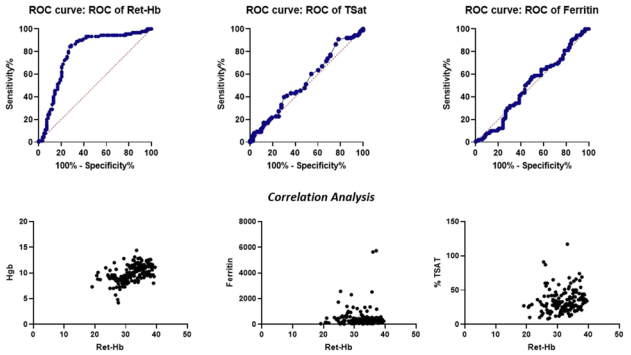
Back ground: Iron deficiency (both absolute and functional) is the main cause of failure to respond to erythropoietin (EPO) in dialysis patients. Traditional laboratory markers, ferritin and transferrin saturation (TSat), are the most commonly used. However, they have significant limitations in this patient population necessitating other parameters to improve the identification of an iron-deficient state.
Objective: The purpose of this study is to compare the performance of reticulocyte hemoglobin (Ret-Hb) with currently used indices of iron sufficiency in rHuEPO-treated dialysis patients.
Methods: Retrospective chart review, 174 samples in 37patients clinical data and laboratory results including Hemoglobin, RET-Hb, and serum ferritin and TSat-were reviewed. The diagnostic performance and optimal cutoff values were determined by receiver operator curve (ROC) analysis.
Results: Two groups were classified: Anemia (<10mg/dl), Non anemia group (>10 mg/dl).All other causes of anemia were excluded and all the patients are on erythropoietin. ROC curve analysis revealed AUC of 0.788 ($P < .0001$) at cutoff 30 pg, by which anemia was discriminated with 93.3% sensitivity and 56.63% specificity, 41% PPV, and 96% NPV. ROC curve analysis

for Tsat and ferritin revealed AUC of 0.54 and 0.50 respectively. We found a positive correlation between Ret-Hb and hemoglobin (r=0.54, p<0.001), between Ret-Hb and transferrin saturation (TSAT) (r=0.24,P=0.0018) .The correlation between Ret-Hb and ferritin is not statistically significant.(r=0.037,P=0.63)



Conclusion: The present study showed that Ret-Hb in comparison to the conventional hematological and biochemical markers commonly used to diagnose iron deficiency is a better diagnostic test of choice

Haemodialysis and peritoneal dialysis

P2-324 - Evaluation of Protein-Energy Wasting in Pediatric Chronic Dialysis Patients

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Introduction: Protein–energy wasting (PEW) in end stage kidney disease (ESKD) is the consequence of a combination of insufficient nutrient intake, uremic toxins, inflammation, and superimposed catabolism. The diagnosis of PEW is based upon biochemical measures, anthropometric parameters, and dietary history. In pediatric dialysis patients, growth is a sensitive marker of nutritional adequacy.
We assessed patient growth using the Gomez and Waterlow criteria. The Gomez classification assesses the percentage of reference weight for a patient's age, and delineates normal, mild, moderate, or severe malnutrition. The Waterlow classification uses the same rating scale as the Gomez classification for the patient's weight-for-height to assess the degree of wasting and the patient's height-for-weight to assess the degree of linear growth stunting.
Methods: Over a 3-month pilot period, we assessed growth for 15 pediatric patients on chronic dialysis, either peritoneal dialysis (PD) or hemodialysis (HD), using the Waterlow and Gomez classification systems. The results of these were compared with serum albumin, growth percentiles, and dialysis adequacy metrics.
Results: When comparing their 3 month averages, there was 1 patient with inadequate total Kt/V and 4 patients with inadequate serum albumin. No patients had a body mass index (BMI) below the 3rd percentile. The Gomez classification noted protein-energy malnutrition in 10 of 15 patients (67%), six of whom with appropriate Kt/V and serum albumin. The Waterlow classification noted stunting in 11 of 15 patients (73%), and 2 of 15 patients (13%) had evidence of wasting.

Patient	Modality	BMI (%ile)	3 Month Average		Gomez Classification	Waterlow Classification	
			Total Kt/V	Albumin (g/dL)	Malnutrition	Wasting	Stunting
1	PD	34.9 (97)	2.88	3.43	Normal	Normal	Moderate
2	PD	N/A	3.62	3.53	Mild	Normal	Moderate
3	PD	25.4 (92)	2.12	4.13	Normal	Normal	Moderate
4	PD	20.6 (49)	3.37	4.03	Mild	Normal	Mild
5	PD	16.5 (24)	2.64	4.13	Mild	Normal	Mild
6	PD	14.8 (12)	2.24	3.83	Moderate	Mild	Moderate
7	PD	22.1 (62)	2.78	3.37	Mild	Normal	Normal
8	PD	17.2 (24)	2.29	3.63	Moderate	Mild	Mild
9	PD	22.5 (61)	1.92	4.33	Normal	Normal	Normal
10	PD	31.7 (99)	2.46	3.57	Normal	Normal	Normal
11	HD	20.7 (50)	1.60	3.70	Mild	Normal	Moderate
12	PD	16.5 (65)	2.33	3.47	Mild	Normal	Moderate
13	PD	N/A	3.31	3.27	Mild	Normal	Moderate
14	HD	21.1 (51)	2.52	4.03	Mild	Normal	Mild
15	PD	17.1 (58)	2.55	3.90	Normal	Normal	Normal

BMI and percentiles for age >2, N/A if age <2; Kt/V adequate if >1.8
Albumin reference range >4.0 g/dL for age 2 and below, >3.5 g/dL for age above 2

Conclusions: In pediatric patients undergoing chronic dialysis, dialysis adequacy, serum albumin, and anthropometric percentiles, are insufficient to fully assess their nutritional status. The addition of growth assessments provide additional insight into a patient's nutritional status and potential need for intervention, and also detect patients with inadequate nutrition that would be missed by standard measures.

ISPD-IPNA Joint Session

P2-325 - Encapsulating peritoneal sclerosis in paediatric patients on long-term peritoneal dialysis

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Objectives: Encapsulating peritoneal sclerosis (EPS) is a devastating complication of long-term peritoneal dialysis (PD) resulting in the need to convert to haemodialysis. This study aimed to determine predictors of EPS in paediatric patients on long-term PD.
Methods: All paediatric patients on PD ≥ 5 years between 2000-2021 at the National University Hospital Singapore were included in this retrospective study. EPS was defined by membrane failure (ultrafiltration of <400ml with 4h dwell of 2.5% dialysate) and clinical and radiological features of intermittent or continuous intestinal obstruction due to peritoneal membrane thickening. The membrane transporter status was evaluated using standard peritoneal equilibration tests within 6 months of PD initiation and at 5 years. Stepwise multivariate logistic regression model including age at dialysis initiation, gender, PD vintage, cause of kidney failure, membrane transporter status at 5 years and number of peritonitis episodes was performed with EPS as the dependent variable.
Results: 40 patients (23 males), median age of dialysis initiation 13.7 years (0.2–23.3 years) and median PD vintage 8.0 years (5-14 years) were included in the study. 5 patients (12.5%) had EPS. Median PD vintage was 9.75 (7.95-13.97) years and 7.86 (4.45-11.00) for EPS versus non-EPS groups respectively (p=0.03). Peritonitis rates in the EPS vs non-EPS group was 0.31 and 0.20 episodes per patient-year respectively (p=0.58). In the EPS group, 4 (80.0%) had HA/H transporter status vs 17 (54.8%) in the non-EPS group (p=0.38). On stepwise multivariate logistic regression, PD vintage was a significant predictor of EPS (OR=1.84, 95%CI 1.06,3.18; p=0.029).
Conclusions: Although HA/H transporter status at 5 years was seen more commonly in patients who subsequently developed EPS, PD

vintage remained a significant risk factor for EPS. Early kidney transplantation should be advocated in paediatric PD patients to avoid this complication.

Haemodialysis and peritoneal dialysis

P2-327 - Epidemiological, social, economic, clinical and survival profile of children and adolescents on peritoneal dialysis at a single center

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Introduction: Chronic kidney disease (CKD) is a clinical syndrome secondary to changes in partial or complete renal function. Peritoneal dialysis (PD) is the first-choice modality in the pediatric population. The objective was to describe a population of children and adolescents at a single pediatric center from 2008 to 2020, to learn about their epidemiological, socioeconomic, clinical profile and to identify associated factors the risk of death.
Methods: Retrospective observational and descriptive cohort study. All patients who started PD in the period from 01/01/2008 and 01/12/2020, from 0 to 17 years and 11 months, with at least three consecutive months of follow-up were included. Data collection was carried out through consultations to the database and medical records of patients. The statistical tests used were: survival curve, Friedman's test, Chi Square, mean and standard deviation or median and quartiles according to the normal or non-normal distribution of the variables, respectively.
Results: Of the 55 children, 65.5% were male and the median age was 2yr. Congenital abnormalities of the kidney and urinary tract (CAKUT) were the main cause of CKD (35%). 54.5% lived outside Belo Horizonte, 70.9% received between 1 and 5 minimum wages. The source of payment for DP was SUS in 91%. Regarding deaths, 45% were due to sepsis. The survival rate was 80%. Among the factors associated with death, the youngest age (3yr *versus* 0.5yr, p=0.008) and low residual diuresis (500ml, *versus* 200ml, for patients who died; p=0.047) were the main factors.
Conclusions: PD in children represents one of the greatest challenges for the multidisciplinary team. The management of patients with younger age and low residual diuresis can represent a major challenge potentially associated with risk of death. Knowing and identifying the characteristics of this population is important to improve care through preventive actions, with a focus on improving survival.

Haemodialysis and peritoneal dialysis

P2-328 - Pediatric peritoneal dialysis in Brazil: document by the Brazilian Society of Nephrology, Brazilian Society of Pediatrics, Brazilian Association of Organ Transplantation, and the Brazilian Association of Dialysis and Transplant Centers.

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Introduction: Acute and chronic kidney dysfunctions are common occurrences in tertiary care pediatric units and are unequivocally associated with morbidity and mortality. The therapeutic approach includes conservative measures and, in advanced cases, renal replacement therapy (RRT). The sustainability of RRT has generated discussions in different geographic regions of the planet, especially peritoneal dialysis (PD), intermittent and slow hemodialysis (HD) and continuous methods of blood purification. This brief communication aims to show data from Brazilian centers that use PD in pediatrics.
Method: Cross-sectional, observational and descriptive study using an electronic survey with 10 questions about PD, widely disseminated between August 11 and 19, 2021. Patients aged 0 to 18 years on PD registered in the databases of the various centers were included. Surveys were filled out anonymously and there was no patient identification data. The study adopted the quantitative methodology.
Results: Sixty dialysis centers answered the questionnaire, of which 23 centers do not have a pediatric program. Overall, 212 patients are currently (August, 2021) on PD in Brazil, 80% of whom are under 12 years of age. The vast majority undergo automated peritoneal dialysis (APD) and 74% are dependent on the Public Health System (SUS). In 25% of services, there was a shortage of supplies in the last six months. In 51% of centers, pediatric patients were converted from peritoneal dialysis to hemodialysis.

Conclusion: Most pediatric patients on PD in Brazil are under 12 years of age and depend on the Public Health System, and shortage of supplies happened in 25% of centers in the last six months. These data bring a call for action regarding the sustainability of the PD program, which is the only alternative to RRT in very young children

Haemodialysis and peritoneal dialysis

P2-329 - Benefits of BNP/NT-proBNP serum level evaluation for dry weight adjustment in paediatric haemodialysis patients

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Background: Dry weight (DW) adjustment in children on haemodialysis (HD) can be challenging. It relies on clinical evaluation and additional supports. Our aim was to study the benefits of cardiac biomarkers assessment, in addition to the more commonly used technique bioimpedance spectroscopy (BIS) and clinical signs for DW prescription in paediatric HD patients.
Methods: Prospective observational study including 41 children on HD in three paediatric HD centres in the Paris region. During one session, BIS was performed before the session and serum levels of BNP and NT-proBNP were analysed before and after the session.
Results: Median pre-dialysis level of BNP was 87 ng/L [24–192] and NT-proBNP 968 ng/L [442–4828]. Cardiac biomarker levels showed positive correlation with the BIS hydration status evaluation (p=0.004). The most appropriate cut-off for pre-dialysis BNP to detect significant overhydration (OH) was 165 ng/L (sensitivity 0.67, specificity 0.84). Based on the BIS evaluation, only 32% of patients with high blood pressure (BP) had OH, whereas in the normal BP group, 33% had significant OH.
Conclusion: DW prescription for children on HD should not only rely on clinical evaluation, particularly BP, and should include additional helpful parameters. BIS is well validated in children, but it has limitations in non-cooperative patients, and its cost can limit its use in some teams. Cardiac biomarkers, especially BNP, were well correlated to hydration status evaluated by BIS, and thus could add valuable information for individual patient management and dry weight assessment.

Haemodialysis and peritoneal dialysis

P2-330 - A case of COVID -19 infection complicated with brain damage in a child on HD

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Introduction: Patients with chronic kidney disease (CKD) are frequently afflicted with neurological complications. Common neurological complications in CKD include stroke, cognitive dysfunction, and encephalopathy, peripheral and autonomic neuropathies. These conditions have significant impact not only on patient morbidity but also on mortality risk through a variety of mechanisms. Acute ischemic stroke is a known neurological complication in patients with respiratory symptoms of COVID-19 infection. Understanding the pathophysiological mechanisms of these conditions can provide insights into effective management strategies for neurological complications.
Case: A 10-year old boy come to our hospital with nausea, vomiting, generalized seizures and altered mental status. Initial vital signs were as follows: Weight 29kg, Height 142cm, temperature 36.6, BP 160/100, SpO2 90%. Previous history: he was diagnosed with RPGN complicated to ESRD and he was on HD for 6 month. One week ago, he got positive COVID-19 test result, and hospitalized to specialized COVID-19 hospital, then discharged with negative PCR test result. Laboratory findings: WBC13.50 10*3/uL, RBC 4.96 10*6/uL, Hb132g/dL, Ht 37.3%, Plt24810*3/uL, Neut10.48, ESR 15. AST102U/L, ALT27U/L, Urea31.1mmol/L, Crea685umol/L, pH- 7.24; pCO2- 35.1; pO2- 61.6; HCO3- 15.4. On day 2 of hospitalization he got into a coma first stage with bulbar syndrome. MRI findings were as follows: subcortical ischemia areas of cerebellum, forehead and both temples, partial angio-encephalopathy and atrophy of the cortex of both hemispheres. He treated with IV mannitol before daily HD. His brain function totally recovered after one month. **Conclusion.** Acute encephalopathies may be caused by a wide variety of metabolic and pharmacologic exposure common in CKD and require rapid treatment to avoid escalation to seizures or coma.

Haemodialysis and peritoneal dialysis

P2-331 - Improvement in exercise functional capacity with an intradialytic exercise program

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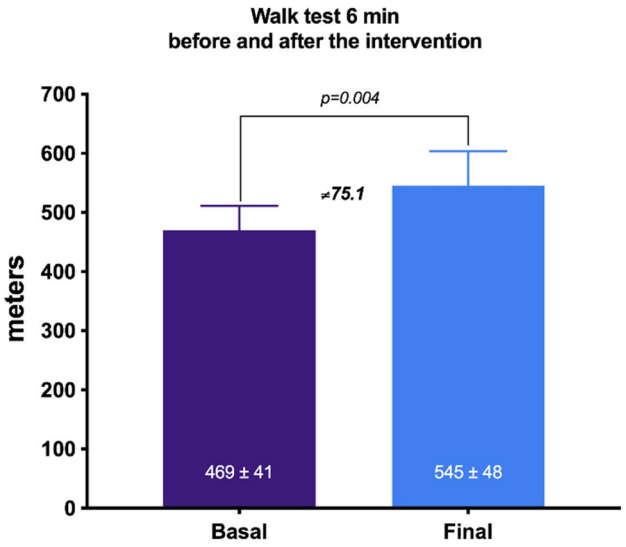
Introduction: CKD is associated with reduced physical activity by several factors, leading to a reduced exercise functional capacity. Intradialytic exercise programs are proved to be feasible and safe to increase functional capacity in adults. However, there is a lack of information on these intradialytic exercise programs in the pediatric population. The six-minute walk test (6MWT) is an established measure of exercise functional capacity in adults and children with CKD. The aim of our study was to evaluate the change in exercise functional capacity according to a 6MWT with an intradialytic exercise program.
Methods: Prospective, single-center study performed in the HD Unit at Instituto Nacional de Pediatría located in Mexico City, Mexico. Twelve prevalent HD patients were enrolled in an aerobic intradialytic exercise with static cycling for 30 minutes 2-3 times per week. Functional exercise capacity was assessed with a 6MWT. The 6MWT was performed on a 10-meter track in a straight hospital corridor at a self-chosen walking speed. Every 2minutes period measurements of respiratory and heart rate, blood pressure, and oxygen saturation were obtained. The primary outcome was the change in functional exercise capacity at baseline and the end of the program (12 weeks).

Results: Of the 12 patients enrolled, 4 patients left the study (fractures non-exercise related, post-surgery complications, kidney transplant, and long-stay hospitalization). A total of 8 patients completed the study, 50 % were female, mean age14.8± 1.4 years, 38 % received twice-a-week sessions. KTv (2.1±0.9), and Hemoglobin levels (11±0.4g/dL) were stable over time. Baseline 6MWT was 469±41 meters, and 6MWT was 545±8 meters after 12 weeks; p <0.004 (Figure 1). There were no adverse events associated.
Conclusion: Our results show improvement in exercise functional capacity, proving that implementing an intradialytic exercise program is safe, feasible, and time beneficial in the pediatric population.



Haemodialysis and peritoneal dialysis

P2-332 - Comparison of cuffed and uncuffed catheter-related bloodstream infection rates in small hemodialysis patients.

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Introduction: Catheter-related bloodstream infections (CBSI) are among the most common and significant complications in pediatric hemodialysis patients. A cuffed long-term central venous catheter (CVC) is recommended when arteriovenous fistula (AVF) formation is not feasible in small patients. We aimed to compare the CBSI rates before and after introducing cuffed CVCs.
Patients and methods: all patients who were unsuitable for AVF formation and received maintenance hemodialysis at our center for more than three months using a cuffed indwelling CVC were included in the study. There were three boys and one girl with a median weight of 14.0 kg (12.4–17.1). Cuffed silicone Hemo-Cath® LT 8F and 10F x 18cm catheters (Medcomp Inc., Harleysville, USA) were used in all cases. The CBSI rate was calculated, and the results were compared with a well-matched historical cohort of our patients before introducing cuffed CVCs. Data were collected retrospectively by reviewing the patients' medical records and analyzed by using descriptive statistics. There were no differences regarding dialysis equipment and catheter handling between the groups.
Results: Eleven CBSIs occurred between March 2016 and March 2022. The total duration of cuffed CVC usage was 4901 days, yielding a CBSI rate of 2.2/1000 catheter days. The median duration of dialysis treatment per patient was 1154 days (367–2225). Twelve catheter revisions were performed, either due to infection or malfunction of the CVC in 41.7% and 58.3%, respectively. The CBSI rate in our historical cohort with uncuffed CVCs was 7.7/1000 days. A 71.4% reduction in the CBSI rate was achieved with cuffed CVCs. The median infection-free catheter survivals for cuffed and uncuffed CVCs were 150 days (14–1524) and 59 days (21–427), respectively (p=0.033).
Conclusions: In our small patients, the CBSI rate associated with cuffed CVCs was significantly lower than in our unit's previously published outcome analysis when uncuffed CVCs were used.

Haemodialysis and peritoneal dialysis

P2-334 - Hemoperitoneum caused by retrograde menstrual flow in an adolescent girl with end stage renal disease receiving peritoneal dialysis

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Introduction: The blood stained peritoneal dialysate (hemoperitoneum) is not an uncommon event in patients receiving PD. It may be related to the peritoneal dialysis catheter or procedure, infection, the underlying renal disease or may be due to factors unrelated to renal disease.
Case History: A 13 years old girl with ESRD following lupus nephritis was started on automated PD three months back. She presented with blood stained PD effluent without any other symptoms. The patient's vital signs were normal. The abdomen was soft and non-tender without any organomegaly. The exit site was healthy.
The peritoneal fluid culture was negative. The inflammatory markers and clotting profile were normal. The platelet count was 233,000/µl and Hb level was11.6g/dl. Ultrasound scan of the abdomen /pelvis was normal without any ovarian cysts or renal cysts. The catheter tip was seen in situ in the pelvis.
The several rapid exchanges were performed and each effluent became less blood stained. The next day, her menstrual period was started. The short cycles (two hour) were introduced and heparin was added to PD fluid to minimize the catheter blockage. As the menstruation ends, the hemoperitoneum settled gradually. The child was discharged with regular PD prescription.
Discussion and Conclusion: The gynecologic events, either physiological or pathological, are by far the most common cause of hemoperitoneum in adult female PD patients. In the reproductive age group, hemoperitoneum from physiological events of the menstrual cycle (either retrograde menstrual flow or ovulation causing mid-cycle bleeding) outnumbers other events. A very small amount of blood (<1 mL) is enough to make 2 liters of peritoneal dialysate appear blood-tinged.
Assessment of the etiology may range from a simple history with a few rapid exchanges to an invasive procedure such as laparotomy or laparoscopy. Once excludes the major pathological condition, the patient should be reassured of this benign self-limiting condition.

Haemodialysis and peritoneal dialysis

P2-335 - Chronic hemodialysis in children under 20 kg – technological challenges

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Introduction: Recent improvements in hemodialysis (HD) technology have improved both the tolerance and efficiency of dialysis sessions in older children and adults. However, over 30% of incident hemodialysis patients enrolled in the International Pediatric Hemodialysis Network and ERA/EDTA registries weigh <20kg and 10% <10kg at inclusion.
Methods: Review of chronic HD devices for children that are available in Europe.
Results: Currently, no device is certified by the European Community for chronic HD in children weighing <10kg. The Fresenius 6008® HD machine is the only one certified for use in children 10 to 20kg, but requires an extracorporeal blood volume of ≥100ml, safely achieved only in children >12kg. Moreover, this device cannot perform single needle treatment, urea clearance and sodium transfer monitoring, or automatic control of ultrafiltration, temperature and sodium transfer in children <40kg. Similarly, the evaluation of vascular access recirculation by this machine requires a blood flow rate ≥100-250ml/min. The Nikkiso DBB-EXA® device is certified for use in children ≥20kg with an extracorporeal blood volume ≥160ml. The Baxter AK98® and Artis-Physio® devices are certified for use in children ≥25kg, with an extracorporeal volume ≥53 and ≥149ml, respectively. AK98® cannot perform online-hemodiafiltration, single needle dialysis, urea clearance monitoring, residual blood volume and vascular access recirculation measurement. UF accuracy of these two devices is ±50ml/h or ±2.5% of the accumulated UF volume, whichever is largest.
Although some Continuous Kidney Replacement Therapy (CKRT) devices can operate with low extracorporeal blood volumes (≤72ml) they have very low dialysate flow rates (≤67ml/min), disqualifying their use for chronic intermittent HD and they do not enable single needle treatment.
Discussion: Inadequate technology restricts optimal HD treatment in the youngest and most vulnerable children. We ask for support from health authorities and industry to improve dialysis treatment, bringing it on par with the high quality of care offered to adult patients.

Haemodialysis and peritoneal dialysis

P2-336 - Studying and Comparing the Effect of Hemodialysis Modalities in Children with Stage 5 Chronic Kidney Disease (CKD5d) on Liver Transaminases

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Background & Aim of the Study: Some studies have shown that hepatitis free adult patients with chronic kidney disease (CKD5) on conventional hemodialysis (HD) have lower serum levels of liver enzymes than controls with normal renal function that might need to modify the reference values in those patients. Do children behave like adults? We tried to answer this question in this study.
Subjects & Methods: We measured and compared the serum levels of liver transaminases; ALT and AST for 85 subjects; 39 on hybrid dialysis (alternating sessions of Online Hemodiafiltration (OL-HDF), 13 on HD and 33 healthy controls, all were age and sex matched. Hybrid and HD groups had comparable duration and frequency of dialysis. All subjects had negative history of hepatitis or any liver disease with negative hepatitis markers.
Results: Serum ALT and AST were significantly lower in both pre dialysis (17.08±9.54 IU/L, 22.92±13.81 IU/L) and post dialysis (15.65±8.65 IU/L, 22.67±12.77 IU/L) samples respectively compared to controls (33.76±6.78 IU/L, 34.12±6.86 IU/L) ($p<0.001$). Post dialysis ALT decreased significantly compared to pre dialysis value ($p=0.006$), meanwhile pre and post dialysis AST were comparable. ALT and AST were comparable across hybrid and HD groups. Regression model and ANOVA revealed highly significant statistical evidence of a positive relationship between pre dialysis ALT as an independent variable and post dialysis ALT as a dependent variable ($t= 3.97$, $p < 0.001$, $R2 = 0.186$, $B= 0.39$).
Conclusion: Children with CKD5 on hemodialysis treatment have lower serum levels of ALT and AST compared to their healthy peers, a finding that could raise the need for establishing separate reference ranges of ALT & AST in these patients to facilitate the diagnosis, monitoring, and treatment of liver diseases in them.
Keywords: ALT, AST, CKD5d, HD, OL-HDF

Haemodialysis and peritoneal dialysis

P2-337 - Desperate Times Call for Desperate Measures: Extra-anatomical Veno-venous Surgical Bypass to Salvage Ipsilateral Arterio-venous Fistula in A Child on Chronic Haemodialysis with Central Vein Occlusion

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During the past two decades, the incidence of CKD in children has increased steadily and even in children, native arteriovenous fistula (AVF) remains as the hemodialysis access of choice. Nevertheless, maintaining a well-functioning fistula is limited by central venous occlusion due to widespread use of central venous access devices prior to AVF creation. Scanty reports are found in literature on successful similar surgical bypass to salvage hemodialysis access among adult patients with central vein occlusion. Here in, we report a successful axillary- external iliac vein bypass in a child with central venous occlusion to maintain her existing brachio-cephalic fistula. Postoperatively, the child received double antiplatelet agents with no bleeding complication. Parents are child empowered to be aware of pressure changes during dialysis. At the time of writing, the fistula continued to function well. This is the first case report in English literature on surgical bypass in a child on hemodialysis. Such drastic measure was inevitable to preserve lifeline and to help patient continue to live well on dialysis when kidney transplantation is scarce.
Conclusion: Extra-anatomical veno-venous surgical bypass is a feasible option to consider even in children. IIn the discussion, we highlight the important factors to preserve the patency of the veno-venous bypass graft based on the literature review. n the discussion we have

highlighted important factors attributing to longer patency of vein-vein to bypass graft based on literature review.

ISPD-IPNA Joint Session

P2-339 - Office and home auscultatory blood pressure measurements show poor concordance with ambulatory blood pressure in children receiving peritoneal dialysis

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Objectives: There are few data evaluating agreement of home blood pressure (BP) and standardised office BP measurement with 24-hour ambulatory BP monitoring (ABPM) on peritoneal dialysis (PD).
Methods: Children aged ≥5, receiving PD over 6-years. Retrospective single centre review of (i) standardised auscultatory office BP performed on the same day as (ii) 24-hour ABPM; and (iii) 7-day mean auscultatory home post- dialysis BP (HPostD_BP) performed by parents. Elevated BP measurements defined as systolic or diastolic BP >90th centile normative values (per 2016 ESH Guidelines).
Results: 24 children (12 boys), median age 13.2 years(range 5.1-17.6), 2-11 months post commencement of PD. 71% on anti-hypertensives. Overall, in office, 17% of SBP and 25% of DBP were elevated. Whilst, following HPostD_BP, 29% SBP and DBPs were elevated. Using 24-hour ABPM, elevated SBP was 25%, 29% and 58% and elevated DBP was 44%, 40% and 44% for 24hr, daytime and night-time BP measurements respectively. Only 42% office SBPs were elevated when HPostD_SBPs were elevated. Conversely ¾ of HPostD_SBPs readings were elevated when office SBP readings were elevated. Only one patient showed both elevated home and office DBP readings. There was masked systolic hypertension in 17% patients looking at HPostD_BPs and in 15% of office readings with masked diastolic hypertension present in 29% office readings and in 50% patients where HPostD_BPs diastolic readings available. White coat systolic hypertension was present in 35% patients per HPostD_BP readings (none on office readings). White coat diastolic hypertension was detected in 50% of those with elevated office measurements and in 40% patients of those with elevated home readings. Conclusion: We present initial data in clinically stable children receiving PD comparing agreement categorising for elevated BP. The clinical utility of HPostD_BP monitoring in patients on PD may be more limited than currently considered and needs evaluating in larger prospective studies.

Haemodialysis and peritoneal dialysis

P2-340 - Variations in urea distribution volume (Vurea) by bioimpedance spectroscopy based on different anthropometric equations in pediatric patients receiving hemodialysis

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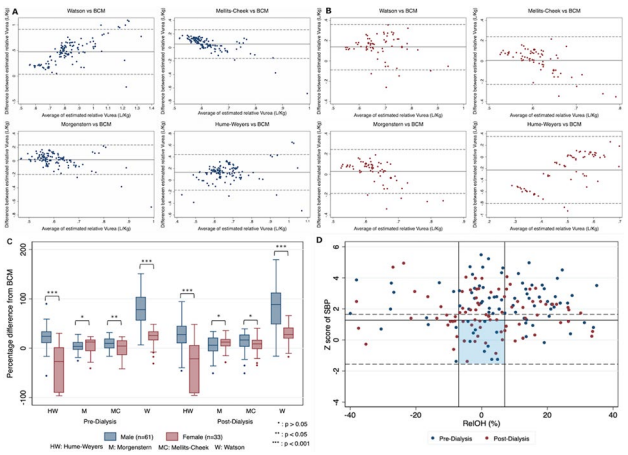
Introduction: Body composition monitoring (BCM) based on bioimpedance spectroscopy is a reliable and non-invasive measure of fluid overload in adult patients on hemodialysis. Assessing urea distribution volume (V_{urea}), integral to this evaluation, relies on anthropometric equations in children. There is limited evidence on the precision of these equations *versus* BCM in estimating V_{urea} in pediatric patients on hemodialysis.

Methods: BCM was performed before and following consecutive sessions of hemodialysis in pediatric patients with acute kidney injury or chronic kidney disease. V_{urea}, estimated from the Morgenstern, Mellits-Cheek, Watson and Hume-Weyers equations, was compared to that derived by BCM, using Bland-Altman analysis. Relative overhydration (Rel-OH; present if >+7%) and relative-V_{urea} (V_{urea}/dry weight) were examined in relation to hypertension (systolic blood pressure, SBP, >95th centile).
Results: BCM was performed in 94 sessions of hemodialysis in 32 patients (68.8% boys) of median (interquartile range) age 110 (72-153) months. All anthropometric equations overestimated relative-V_{urea}, except the Hume-Weyers equation that underestimated it in post-dialysis measurements in girls. The least mean difference of relative-V_{urea} to BCM was for the Morgenstern equation in boys [0.017 (-0.201-0.234) L/kg] and Mellits-Cheek equation in girls [0.005 (-0.231-0.240) L/kg]. The mean percentage difference of relative-V_{urea} in pre- and post-dialysis measurements differed significantly between genders for the Watson and Humes-Weyers equations. Hypertension was present in 64.4% and 40.2% of the pre- and post-dialysis measurements, respectively. However, only 46.4% and 45.5% of the patients in the respective measurements were assessed as overhydrated. Relative overhydration did not correlate with SBP standard deviation scores (r=0.054; P=0.48).
Conclusion: V_{urea} derived from different anthropometric equations varies significantly from BCM-derived value, and systolic hypertension does not correlate with Rel-OH. BCM requires validation in larger studies on pediatric patients.



ISPD-IPNA Joint Session

P2-341 - Effect of extracellular vesicles from peritoneal dialysate on the progression of peritoneal dialysis associated peritoneal fibrosis

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Extracellular vesicles (EVs) have been widely studied for the treatment of lung, kidney, skin or heart fibrosis in preclinical and clinical trials. However, only a few, mainly proteomic studies investigated the EVs of peritoneal dialysate (PDE). Therefore in the present study we investigated the role of PDE-EVs on the pathomechanism of peritoneal fibrosis. PDEs were collected from children receiving peritoneal dialysis treatment in the Ist Department of Paediatrics, Semmelweis University, Hungary. PDE-EVs were isolated by size exclusion chromatography following ultrafiltration and were characterized according the recommendations of the International Society for Extracellular Vesicles. Their significance on the viability and LDH release of human primary peritoneal mesothelial cells (HPMC) and human umbilical vein endothelial cells (HUVEC) treated with methylglyoxal (MGO) or hydrogen peroxide (H2O2) was tested by MTT or LDH assay, respectively. Expression of antioxidant genes was measured by real-time RT-PCR . Effect of EVs was also studied in a MGO induced mice model of peritoneal fibrosis *in vivo*. Submesothelial thickness was analysed after Masson's Trichrome staining and peritoneal transport was monitored using tetramethylrhodamine isothiocyanate-dextran.
PDE-EVs showed typical EV features and penetrated into the cytoplasm of HPMC and HUVEC cells as well. According to the MTT and LDH assays PDE-EVs prevented H2O2- or MGO-induced cellular damage. Furthermore, PDE-EVs reduced the expression of antioxidant genes, including heme oxygenase (*hHO) 1* and glutamate-cysteine ligase catalytic subunit (*hGCLC)* of MGO treated cells. In vivo, the intraperitoneally administrated PDE-EVs entered into the cells of the peritoneal membrane of C57BL/6J mice and reduced the MGO treatment induced peritoneal thickness and improved ultrafiltration capacity of the peritoneal membrane.
In summary, PDE-EV reduces the harmful effect of H2O2 or MGO treatment *in vitro*, moderates submesothelial thickening and ameliorates the ultrafiltration capacity of the peritoneal membrane *in vivo*.
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Haemodialysis and peritoneal dialysis

P2-342 - Acute hemodialysis experience in pediatric patients weighing less than 15 kg

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Objectives: There are few studies on the prognosis of pediatric patients who have received renal replacement therapy (RRT). This study aims to examine the clinical features of patients who have undergone acute RRT while weighing less than 15 kg.
Methods: Patients who have undergone acute RRT while weighing less than 15kg with a minimum follow-up period of 6 months were included. Survived patients were examined at the last visit.
Results: A total of 80 patients (42 female, 38 male) were included in the study. Among them, 43 patients (53.8%) received hemodialysis (HD) and 37 patients (46.2%) received peritoneal dialysis (PD). The age, height, weight, and body surface area of HD patients were found to be significantly higher than those of PD patients ($p<0.001$). Most of the patients less than 5 kg (96%) received PD and most of the patients between 10.1-15 kg (88.6%) received HD. At the end of the dialysis process, 41 patients (51.3%) survived. It was determined that the height, weight, and body surface area values of the surviving patients at the beginning of dialysis were higher than those of the deceased patients ($p<0.001$). In multiple regression analysis, only low weight and vasopressor treatment were found to be negatively associated with survival. Dialysis modality did not affect survival. At the last visit, 31 patients could be evaluated. Non-nephrotic proteinuria was found in six (19.3%) of 31 patients (38.8%). Stage 2 chronic kidney disease (CKD) was diagnosed in three patients (9.6%). Office blood pressure measurement revealed hypertension in one patient. Masked hypertension was detected in one patient with 24-hr ABPM.
Conclusions: PD and HD can be used safely, and effectively in patients weighing less than 15 kg. Findings such as CKD, proteinuria, and hypertension may be observed in these groups of patients and they should be followed up regularly.

Haemodialysis and peritoneal dialysis

P2-343 - Retrospective analysis of complications of hemodialysis treatment in children with chronic kidney disease

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Objective: To analyze the complications in children's hemodialysis, summarize the symptoms and complications during children's hemodialysis, and provide prevention and treatment methods.
Subjects: From January 2021 to December 2021, children with chronic kidney disease(CKD) underwent hemodialysis in the Children's Blood Purification Center of the First Affiliated Hospital of Jinan University.
Methods: 1. Clinical data of children with CKD undergoing hemodialysis in our hospital collected retrospectively; 2. Statistics and analysis of the incidence of dialysis complications.
Results: Total of 937 dialysis times of children with CKD on hemodialysis were counted in our hospital in 2021. Hypertension was the most common complication during hemodialysis, with an incidence rate of 8.1%, and blood pressure increased 76 times. Hypotension occurred 65 times (7.3%). Imbalance syndrome of dialysis occurred 2 times, and the incidence was 0.2%. In this group of 13 children with hemodialysis status, there were 6 males and 7 females. Long-term dialysis complications occurred, parathyroidism occurred in 5 cases (38.5%). Long-term catheter thrombosis occurred in 2 cases (15.4%). The incidence of mental and psychological disorders was 15.4% in 2 cases. Catheter-related infection is prone to occur in individuals with low immune function, malnutrition and immunosuppressant use, and the incidence rate of 1 case in this group was 7.7%.
Conclusion: In this study, hypertension is the most common complication in children undergoing hemodialysis. Maintaining blood purification dialysis is an important means to maintain the life of children with end-stage renal disease. At present, most children choose long-term deep vein catheterization as vascular access for maintenance dialysis, but infection, thrombosis and other complications caused by long-term catheterization have also become important reasons endangering the life of children.

Glomerulonephritis (including vasculitides)

P2-346 - Review of Acute Post-Streptococcal Glomerulonephritis at the Red Cross War Memorial Children's Hospital, Cape Town, South Africa

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In this retrospective study we describe the occurrence of acute post streptococcal glomerulonephritis (APSGN) among children (<14years) admitted to the Red Cross War Memorial Children's Hospital in Cape Town, South Africa (SA) from January 2015 to December 2020. There were 161 cases of acute nephritic syndrome (haematuria, oedema, oliguria and hypertension), 100 met the inclusion criteria and were recruited. Demographic, clinical features, laboratory findings, management, and outcome data were collected. Data were presented as medians (IQR) or means (SD), while categorical data were presented as proportions. APSGN was defined based on the clinical presentation of at least two signs of acute nephritis, a low serum complement 3 (C3) level or evidence of a recent streptococcal infection. APSGN was more often associated with streptococcal skin infections (55%). Seventy-five (75%) children presented in stage 2 hypertension, with 10 (10%) presenting with hypertensive seizures. C3 levels were low in 86 (86%) children; 94 (94%) children had elevated ant deoxyribonuclease-B (anti-DNase-B) levels, and 80 (80%) also had elevated anti-streptolysin O titre (ASOT) at presentation. A percutaneous kidney biopsy was indicated in eleven (11%) children. Seven (64%) biopsies confirmed type II crescentic glomerulonephritis, and four (36%) showed histological features of post-infectious nephritis. While 62 (62%) children recovered, five (5%) progressed to end stage kidney disease (ESKD). Childhood APSGN remains an important health problem in SA with favourable outcome in most cases apart from those with crescentic glomerulonephritis who progressed to ESKD.

Glomerulonephritis (including vasculitides)

P2-347 - Etiology, pattern of glomerular injury and outcome of children presented as rapidly progressive glomerulonephritis in Bangladesh

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Background: Sometimes children are coming with features suggestive of rapidly progressive glomerulonephritis (RPGN) with variable underlying glomerular injury .
Objective: This prospective study was designed to find out the etiology, histopathological pattern of glomerular injury and outcome of children who presented with RPGN like features.
Methods: Forty two patients age ranged from 2 year to 18 year admitted with hematuria, proteinuria, hypertension and rapid impairment of kidney functions were enrolled in the study over a period of two years. Diagnosis and staging of AKI was based on KDIGO working definition of AKI, clinical assessment, relevant laboratory investigation and kidney histopathological changes.
Results: Out of 42 cases 67% patient had crescent in the glomeruli and 33% presented with the features of RPGN with less severity and without crescent in the glomeruli. Post infectious glomerulonephritis (PIGN) was 36% in the crescentic group and the most common primary etiology of RPGN with crescent followed by IgA nephropathy (14%) and lupus nephritis (10%). The most severe form of AKI was observed in those who had >50% crescent in the glomeruli (29%) and required treatment with hemodialysis along with methylprednisolone. Acute tubular necrosis (ATN) was 12% and the most common cause of RPGN without crescent, followed by PIGN (7%) and Hemolytic Uremic Syndrome (5%). Higher percentage of AKI stage II (28.6%) and stage III (71.4%) had been found in RPGN with crescent group. Significant association of AKI stage III with crescentic GN was found ($p<0.016$). About 62% patient died who had more than 50% crescent and only 15% patient in less than 50% crescent ($p<0.02$) and 14% death in without crescent group.
Conclusion: PIGN was the most common primary etiology of RPGN with crescent. ATN and HUS may present as RPGN but without crescent. Severity of AKI and mortality were significantly higher in crescentic GN.

Glomerulonephritis (including vasculitides)

P2-348 - Efficacy of immunosuppressive therapy compared with standard therapy on kidney outcomes in children with Immunoglobulin A nephropathy: A systematic review and meta-analysis

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Background: Immunoglobulin A nephropathy (IgAN) is the most common primary glomerular disease with nearly 40% of patients reaching kidney failure. IgAN is treated with supportive therapy and immunosuppressive therapy. Supportive therapy include medications such as angiotensin converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB) which reduces urine protein. Corticosteroids is the main immunosuppression for IgAN. Recent trials show that immunosuppression is associated with significant side effects and no improvement in kidney outcomes. Children are more susceptible to side effects from immunosuppression. We need to provide effective medical intervention while minimizing harms. There is no known review of the pediatric literature looking at both RCTs and non-randomised studies of intervention (NRSI) for IgAN management.
Aim: To determine the benefits and harms of immunosuppressive therapy compared with standard treatment on kidney outcomes in children with IgAN through a systematic review and meta-analysis.
Methods: This review protocol is written according to PRISMA-P and will be published on PROSPERO. We will search CENTRAL, MEDLINE, EMBASE, ICTRP and ClinicalTrials.gov databases, and conference proceedings. References from reviews and guidelines will be hand searched. Study selection criteria will include RCTs and NRSI comparing immunosuppression (steroids, rituximab, cyclophosphamide, cyclosporine, tacrolimus, azathioprine, mycophenolate mofetil, mizoribine, leflunomide, fish oil) and standard treatment (ACEi, ARBs) or tonsillectomy, on the kidney outcomes (progression of chronic kidney disease, kidney failure, remission) in children (≤18 years) with IgAN. Two authors will independently determine study eligibility, extract data and assess risk of bias (ROB) for each study. Statistical analyses will be performed using the random effects model and the results will be expressed as risk ratio for dichotomous outcomes and mean difference for continuous outcomes with 95% confidence intervals. Cochrane ROB-2 tool for RCTs and ROBINS-I tool for NRSI will assess ROB. Overall grading of the evidence will be done using GRADE approach.

Glomerulonephritis (including vasculitides)

P2-349 - Pattern and outcome of Glomerular Diseases in Sudanese Children:a Clinico-Pathological Study, Khartoum, Sudan

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Background: Glomerular diseases are the most common cause of chronic kidney disease (CKD) and/or end-stage kidney disease (ESKD) in many countries. In general, the incidence of CKD and renal failure is more common in developing countries than in developed ones
Objective: This study aims to describe the pattern of glomerular diseases in Sudanese children from a clinicopathological perspective.
Methodology: We retrospectively reviewed the clinical records of190children seen with nephritis/nephrosis at the Pediatric Nephrology Unit, Soba University Hospital and Dr Salma Dialysis Centre, Khartoum. during the period from2010 to 2020. Ultrasound-guided Kidney Biopsies were performed percutaneously using a needle size 16G. The biopsy sample was examined for light microscopy and immunohistochemistry and electron microscopy performed abroad in selected cases.
Results: The mean age of the 190 study children was14.3 years (range 2 months-18 yrs) of whom 107..were males (56.3%). the majority of the patient presented with features of nephritis 93(48.9%), followed by nephrotic presentation 60(31.6%) and the least presentation was lupus nephrities.29.The most common glomerular disease encountered was Post Infectious GlomeruloNephrities40(21.8%) followed by Mesangioproliferative GN and focal segmental glomerulosclerosis 36(18.9%), 35(18.4%) respectively. SLE nephritis was in 27(16.1%) (minimal change disease seen in 16(8.4%). 26 samples were examined by immunohistochemistry with the most frequent pattern being IgA Nephropathy seen in 14 cases. Membrane Prolifeartve Glomerulonephrities MPGN was 13(6.8%). HBsAg positive in 8(4.2%)and the most common lesion was FSGS.
Conclusion: The spectrum of glomerular diseases among children varied across sexes, age groups. Renal biopsy remains a critical diagnostic procedure for managing a considerable proportion of renal diseases.

Glomerulonephritis (including vasculitides)

P2-350 - Lupus nephritis: demographics and outcomes in Pakistani children and adolescents, a single center experience

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Background: Kidney involvement and its treatment is a major cause of morbidity and death in patients with systemic lupus erythematosus (SLE), affecting 30%-70% of those in the pediatric age group. Childhood lupus nephritis is a difficult condition requiring expensive testing and drugs as well as frequent follow-up. Pediatric SLE data is lacking from Pakistan and other low middle income countries.
Objectives: A 5-year, single center perspective of children and adolescents with SLE and nephritis.
Methods: The Indus Hospital and Health Network (IHHN) is a tertiary care, free health system with its sentinel site in Karachi, Pakistan. We retrospectively collected data of children (0-19 years) who were diagnosed with SLE and nephritis at IHHN from 2015-2020. Data included patient demographics, presenting complaints, laboratory data (urinalysis, renal function, complement levels, lupus specific serologies, renal histopathology), treatment and outcomes till 2020.
Results: A total of 46 children and adolescents were diagnosed with SLE with a female to male ratio of 5.5:1. More than half the cohort (25/46, 54%) was between 15-19-year age. Of all children with SLE, 23 (50%) had lupus nephritis (LN) and of these 13/23 56.5% underwent a renal biopsy. Children with class III and IV LN accounted for 69% of the biopsied cohort. Overall outcomes following treatment revealed full clinical and lab remission in 39%, residual proteinuria and hypertension in 26%, chronic kidney disease among 13%, loss to follow up in 9% and death in 13% of children and adolescents with lupus nephritis.
Conclusion: Renal involvement with SLE is very common among children and adolescents in our setting and accounts for the associated morbidity and mortality. Our results indicate better overall outcomes compared to available regional data. Timely diagnosis and free of cost management of this chronic complex disease, can improve renal and mortality outcomes in low resource settings.

Glomerulonephritis (including vasculitides)

P2-352 - The role of complement in primary membranous nephropathy

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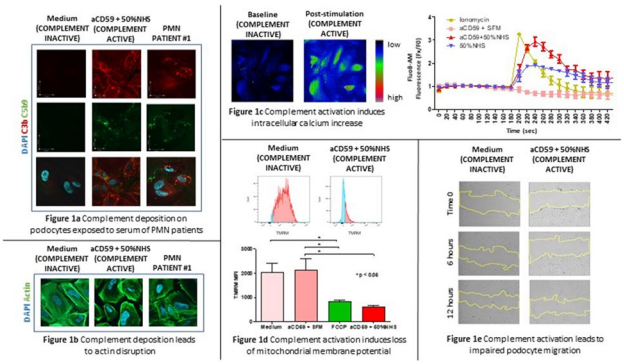
Introduction: Primary membranous nephropathy (PMN) is the leading cause of nephrotic syndrome in adults and a common cause of end-stage kidney disease (ESKD). The Heymann's nephritis mouse model of PMN shows that proteinuria is complement-mediated. However, the pathogenetic role of complement in human PMN remains unclear. Our preliminary data showed that complement deposition (C3b and C5b9) can be detected on podocytes exposed to serum of PMN patients (recruited from the Toronto GN Registry), leading to disruption of actin cytoskeleton (Figure 1a-b). We aim to demonstrate that complement activation can have both structural and functional effects on podocytes.
Material and Methods: An in-vitro model of immortalized human podocytes (from Moin Saleem, Bristol, UK) was used for all the experiments. Cells pre-sensitized with anti-CD59 were exposed to 50% normal human serum (NHS) to obtain complement deposition on the podocytes surface. Subsequently, changes in intracellular calcium levels were monitored using a fluorescent dye (Fluo8-AM), acquiring images every 20 seconds (up to 10 minutes) by confocal microscopy. Calcium effects on mitochondrial membrane potential were measured by flow cytometry using tetramethylrhodamine, methyl ester (TMRM) dye. Wound healing assays were performed to study functional effects on podocyte migration.
Results: Complement activation led to a significant rise in the intracellular calcium levels. Loss of mitochondrial membrane potential was also observed, together with disruption of the actin cytoskeleton and impaired cell migration (Figure 1c-e).



Discussion and Conclusions: Complement is active in PMN, leading to both structural and functional effects on podocytes. Further studies are needed to better understand the consequences on the podocyte energy machinery and the possibility of its reversibility by using complement inhibitors. Our research of such alternate therapy could lead to improvement in outcome in PMN where, despite current therapies, up to one third of patients develops ESKD.

Glomerulonephritis (including vasculitides)

P2-354 - A 2-year-old child with unexpected diagnosis of Lupus Nephritis

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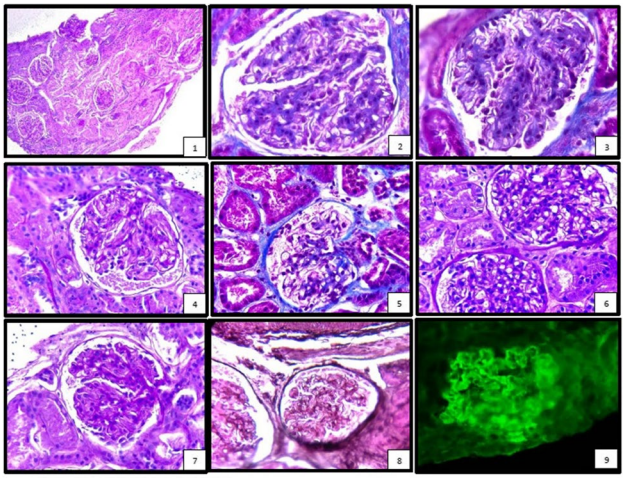
Introduction: The lupus nephritis (LN) is a manifestation of systemic Lupus Erythematosus (SLE) which increases morbidity and mortality. It is most frequently seen in girls (5:1), and the estimated incidence of lupus nephritis is 0.36- 0.9/100,000 children per year, rarely seen before the age of 5.
Case presentation: A 2-year-old male suspected of an autoimmune anemia (HGB 7.5 g/dl, HCT 23.4%, PLT 69 x10^3) was treated by hematology service with prednisone 2 mg/kg/day for one month and without response. The patient presented a progressive deterioration and was admitted to our center on January 14, 2021, finding proteinuria in the nephrotic range (107 mg/m2/hr), hypertension (118/80 mmHg p>99), and hematuria (45-50/c). C3 Levels (69 mg/dL) and C4 (11.3 mg/dL), Ac. Antinuclear HEP 2 positive (3.15 INDEX), Ac. Anti DNA negative (26.58 IU/ml), Ac Anti SM positive (> 40 U/ml). Ultrasound-guided biopsy was performed and reporting class V membranous lupus nephritis. On February 04, 2021, the management proposed was methylprednisolone (10 mg/kg/dose per 5 pulses) and cyclophosphamide (750 mg/m2/dose). In his last control (09/02/2022), hemoglobin values were 11.2 g/dl, hematocrit 33.4%, platelets 406 x10^3, creatinine 0.2 mg/dl and proteinuria 30 mg/dl.



1. HyE: Sin daño crónico túbulo-intersticial.
2. Masson: Engrosamiento difuso y homogéneo de los capilares glomerulares, sin lesiones proliferativas.
3. Masson: Engrosamiento difuso y homogéneo de los capilares glomerulares, sin lesiones proliferativas.
4. PAS: Engrosamiento difuso y homogéneo de los capilares glomerulares.
5. Masson: Sin lesiones proliferativas en glomérulos.
6. PAS: Engrosamiento difuso y homogéneo de los capilares glomerulares.
7. PAS: Engrosamiento difuso y homogéneo de los capilares glomerulares, podocitos prominentes.
8. Jones: Engrosamiento difuso y homogéneo de los capilares glomerulares.
9. Inmunofluorescencia con depósitos mesangiales y subepiteliales.

Discussion: SLE can occur at any age, although its peak incidence in pediatrics is at 12 years, our patient was 2 years old at the time of diagnosis, every patient with suspected autoimmune process regardless of their age, SLE should always be ruled out.
Conclusion: SLE is a pediatric disease that can occur in children under 5 years of age, timely management is the key in preserving kidney function and avoiding future complications. We suggest that SLE should always be considered in patients under 5 year of age.
Bibliography: Hanna Szymanik-Grzelak & Małgorzata Barabasz et al., Retrospective analysis of clinical and pathomorphological features of lupus nephritis in children, Advances in Medical Sciences, Vol 66, Issue 1, 2021, Pages 128-137.

Glomerulonephritis (including vasculitides)

P2-355 - Potency and adequacy of Mycophenolate Mofetil according to Histopathology of Pediatric Lupus Nephritis-A single centre experience

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Background: Survival is worse in childhood onset lupus nephritis but data are relatively scarce compared to adult. Our aim was to evaluate the effectiveness of MMF during induction therapy of pediatric lupus nephritis.
Methods: 42 lupus nephritis children under 18 years were enrolled from July 2017 to Feb 2022. Renal biopsy was classified according to International Society of Nephrology/ Renal Pathology Society. 17 patients had Class IV, 7 patients class II, 4 patients class III and 2 patients had class V. 12 patients did not do biopsy. 32 patients were treated with oral MMF,maximum daily dose 1.2g in 2 divided doses and 10 patients were treated with intravenous Cyclophosphamide as monthly pulse (500-750mg/m2) during induction.
Result: Female male ratio 8:2. Mean age at onset 11years (3-16 years). 19 (45%) patients had renal impairment at the onset. 6 (14%) patients

need dialysis. Diffuse proliferative lupus nephritis was the commonest histopathology. MMF was given in Class II,III,IV and Class V lupus nephritis patients, both during induction and maintenance phase. Cyclophosphamide was given only in class IV patients during induction and MMF was given on maintenance. Along with MMF or Cyclophosphamide all patients were given monthly pulse Methylprednisolon 3 doses for 6 months as well as hydroxychloroquine during induction. Oral prednisolon was continued during maintenance. 9 (21%) patients died during hospitalization and all deceased patient took MMF during induction and 7 were class IV lupus nephritis. Although MMF showed good response in class II,III,V lupus nephritis Cyclophosphamide still superior to MMF in treating class IV lupus nephritis.
Conclusion: Our study concluded that mortality was predominant using MMF during induction therapy having diffuse proliferative lupus nephritis although MMF was considered as a valuable alternative to more cytotoxic regimen. Infection, renal impairment, social status, noncompliance and delayed referral were other factors of unfavourable prognosis in children.
Key words: Children,lupus nephritis, Mycophenolate mofetil

Glomerulonephritis (including vasculitides)

P2-356 - Comparison of Clinical and pathological characteristics among different age groups in childhood-onset lupus nephritis——a multi-center retrospective study

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Introduction: To summarize and compare the clinical and pathological characteristics between different age groups of childhood-onset lupus nephritis (LN).
Material & Methods: Clinical and pathological data of 638 patients with childhood-onset from three pediatric nephrology centers were retrospectively collected and studied. Patients were divided into preschool-, school-age and adolescent group according to age of onset and compared between different age groups.
Results: Of 638 patients with childhood-onset LN, 48 (7.5%), 420 (65.8%) and 163 (25.5%) were preschool-age, school-age, and adolescent, respectively. Fever and rash were more common in school-age group than in preschool-age or adolescent group ($P<0.05$), while alopecia, pleurisy, and edema were more common in adolescent group than in preschool- and school-age groups. Patients in all age groups had severely active SLE with the median SLEDAI score 16 (12, 19). The estimated glomerular filtration rate and serum albumin decreased with age ($P<0.05$). Urinary protein in adolescent group was significantly higher than that in preschool- and school-age groups ($P<0.001$), but there was no difference in the rate of urinary erythrocyte, pyuria, and cellular casts among different age groups ($P>0.05$). Proliferative glomerulonephritis was the most common pathological classification with 19 (48.7%), 185 (58.9%) and 81 (62.3%) cases were type IV in preschool-age, school-age, and adolescent, respectively. The rates of glomerular white blood cell infiltration, balloon adhesion, tubule atrophy, activity index and chronic index in adolescent group were higher than those in school-age group ($P<0.05$).
Conclusion: Patients with childhood-onset lupus nephritis in different age groups presented with different clinical manifestations with similar disease activity and pathological classification.

Glomerulonephritis (including vasculitides)

P2-357 - Comparison of mycophenolic acid with cyclophosphamide for the treatment of pediatric lupus nephritis: a retrospective study from a tertiary center in Taiwan

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Background: This study is aim to compare the efficacy of mycophenolic acid (MPA) and cyclophosphamide (CYC) as treatment in pediatric lupus nephritis (pLN) proved by renal biopsy.
Methods: Patients with pLN class III, IV and V proved by renal biopsy were collected from the Databank of Kaohsiung Veterans General Hospital (KSVGH) between February 2005 and December 2020. Only cases with complete treatment with either MPA or CYC were enrolled. The patients were divided into two groups, MPA and CYC. Demographic data at month 0 were collected. Therapeutic effects included systemic lupus erythematosus disease activity index score (SLEDAI score), laboratory findings, complete remission (CR), partial remission (PR) and no-response (NR) to treatment were assessed at month 6, 12, and 24.
Result: Based on the enrollment criteria, 31 pLN were included. Of the patients, 15 patients received MPA and 16 patients received CYC. The primary endpoint was CR, and the secondary endpoint was PR. In MPA group, CR occurred in 7/15(47%) patients at month 6, 11/15(73%) patients at month 12 and month 24. In CYC group, CR was reached 5/16(31%) patients at month 6, 8/16(50%) patients at month 12 and 9/16(56%) patients at month 24. PR was seen in 3/15(20%) patients in MPA group and 3/16(19%) patients in CYC group at month 24. The cumulative probability of CR and PR showed no statistically significant difference between the two groups at month 6, month 12, and month 24. But, the estimated glomerular filtration rate (eGFR) improved significantly in MPA group at month 6 and month 12 as compared with CYC group ($p < 0.05$).
Conclusion: According to our study, the efficacy of MPA is similar to CYC for pLN treatment. We suggested that MPA has the same efficacy with CYC in the treatment of patients with pLN.

Glomerulonephritis (including vasculitides)

P2-359 - Hyperammonemia in Late-onset ornithine transcarbamylase deficiency caused by steroid administration for IgA nephropathy

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Introduction: Ornithine Transcarbamylase deficiency (OTCD) is one of the urea cycle abnormalitieswhich is associated with hyperammonemia. OTCD usually present at birth up to early childhood, rarely after school age. Late-onset OTCD may develop with hypercatabolism such as infection, starvation,surgery and steroid administra-

tion etc. Here, we report a case of late-onset OTCD in a 10-year-old boy who presented with disturbance of consciousness associated with hyperammonemia during steroid therapy for IgA nephropathy.
Case report: A 10-year-old boy was admitted due to acute gastroenteritis. He had undergone oral steroid therapy for IgA nephropathy 45 days before. He had been vomiting repeatedly five days before and IV therapy were administered three days before. His symptoms continued, which made him not to eat for five days. So he was admitted to the hospital. After admission, he showed abnormal behavior and disturbance of consciousness. Blood ammonia level was high at 824 μg/dL. He was intubated and underwent continuous hemodialysis. However, the level was further elevated to 1024 μg/dL. The dialysis was switched to intermittent hemodialysis, then, the level was decreasing. Next day the level was normalized. He was discharged without major sequelae after three weeks of hospitalization. Genetic analysis led to the diagnosis of OTCD. After discharge, the steroid was tapered off in consideration of the risk of hyperammonia.
Conclusion: Pediatric nephrologists often use steroid therapy for renal diseases. Even after school age, hyperammonemia may occur following steroid administration. In this case, steroid administration and starvation due to gastroenteritis might serve as a trigger of hyperammonemia. We experienced a rare case of OTCD complicated with IgA nephropathy.

Glomerulonephritis (including vasculitides)

P2-360 - Investigation of prognostic factors before starting treatment in mild IgA nephropathy treated with renin-angiotensin converting enzyme inhibitors

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Background: In Japan, using RAS inhibitors (ACEIs) for 2 years is recommended for the treatment of mild pediatric IgA nephropathy. It has been reported that 80% of cases go into remission with this treatment, but we have also experienced cases with a poor prognosis.
Methods: We selected 22 patients with mild pediatric IgA nephropathy who were first treated with ACEI from 1995 to 2015. The definition of mild pediatric IgA nephropathy is as follows: 1) pathological findings such as mesangial proliferation of less than 80% of the total glomerulus. 2) urinary TP / Cr ratio <1.0 g / gCr, 3) normal renal function. These patients were divided into two groups. The (P-) group consisted of patients who reached remission within 2 years. The (P+) group consisted of patients with residual proteinuria and / or those who received another treatment. We compared their prognoses and searched for risk factors.
Results: The P- group consisted of 14 patients and the P+ group, 8 patients. The median total observation period was 5.6 (4.5-10.3) years. There was no difference between the two groups in pretreatment urinary TP / Cr ratio, pretreatment eGFR, or the time period from initial symptoms to the start of treatment. However, the age at the first renal biopsy was higher in the P + group (10.67 ± 2.6 years vs. 13.9 ± 3.3 years, p <0.03). There was no difference in the MEST score before treatment. In two patients in the P + group, urinary protein increased and kidney dysfunction progressed even after the addition of multidrug therapy.
Discussion: It was difficult to predict the prognosis of mild pediatric IgA nephropathy based on clinical and pathological findings before the start of treatment. In adolescent cases, special attention should be paid to the transition of urinary proteins during and after treatment.

Glomerulonephritis (including vasculitides)

P2-362 - Differences between children and adults with primary IgA nephropathy and associated mechanism

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Background: Children and adults with IgA nephropathy (IgAN) are different in clinical pathological manifestations, treatment patterns and long-term prognosis. However, the underlying mechanism is still unknown.
Objectives: To investigate the difference between children and adults with IgAN and explore the associated mechanism.
Methods: Patients diagnosed as primary IgAN were extracted and compared between two multicenter cohorts of adults and children, respectively. Levels of circulating Gd-IgA1, IgG immune complex and MBL were detected by sandwich enzyme-linked immunosorbent assay (ELISA). Staining of C4d, C3d and C5B-9 was performed on kidney tissues by immunohistochemical method.
Results: A total of 996 children and 1768 adults with IgAN were included. Children manifested with significantly more severe proteinuria and hematuria. Pathological analysis revealed a higher proportion of M1(61.9% vs. 39.9%, P<0.001) and E1(41.9% vs. 32% , P<0.001) lesions, and a lower proportion of S1 (28.2% vs. 62.4% , P<0.001) and T1/2 lesions (8.2% vs. 35.2%, P <0.001) in children, compared with adults. Clinically, more children were prescribed with steroids (84% vs. 37.9% , P <0.001). During 2-year follow-up, proteinuria remission was more prevalent in children (82.7% vs. 36.3%, P < 0.001).
No significant difference was found in Gd-IgA1 and IgA-IgG complexes levels between children and adults with IgAN. Whereas children were found with significantly higher circulating MBL levels. The prevalence of glomerular deposition of terminal complement complex C5b-9 in children was higher than that in adults (80% vs. 50%, P=0.05), with stronger staining intensity. Deposition intensity of C4d was significantly higher in children, too.
Conclusion: Compared with adult patients, children with IgAN were significantly more active in clinicopathological manifestations, with better prognosis. It was found that the level of complement activation, especially lectin pathway activation, was significantly higher in children. Our study provides important evidence for targeted therapy in different IgAN populations.
Acknowledgement
We express our gratitude to Registration of IgA nephropathy in Chinese Children Working Group.

Glomerulonephritis (including vasculitides)

P2-364 - Cyclic neutropenia and concomitant IgA nephropathy: A case report study

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Abstract
Background: IgA nephropathy (IgAN) is universally recognized as one of the most common primary glomerular diseases in all ages. The outcome during childhood is generally good, but progression in the long-term follow-up may occur. Cyclic neutropenia (CN) is a rare hematologic disorder, which is associated with mutations of ELANE gene. Cases of concurrent cyclic neutropenia (CN) and IgA nephropathy (IgAN) have been reported only twice. However both studies lack important information.
Case presentation: Here we report the case of a 10-year-old boy who presented with recurrent viral upper respiratory tract infections in combination with several episodes of febrile neutropenia, hematuria, proteinuria and acute kidney injury (AKI). Upon his first admission physical examination was unremarkable. His kidney function was impaired and urine microscopy showed evidence of macroscopic hematuria and proteinuria. Twenty-four-hour urinary collection revealed non-nephrotic range proteinuria of 800 mg. Further workup showed elevated IgA. His histology revealed mesangial and endocapillary hypercellularity with mild crescentic lesions, while immunofluorescence microscopy showed IgA positive staining, consistent with IgAN. Genetic testing confirmed the clinical diagnosis of CN. He was treated initially with an angiotensin-converting-enzyme inhibitor (ACE-I) showing a good response for a period of 28 months. However, due to persistently increased proteinuria above 1g for more than 3 months, corticosteroids (CS) were added according to KDIGO guidelines for a period of 6 months. Granulocyte colony-stimulating factor (G-CSF) was administered to stabilize neutrophil count.
Conclusion: ACE-I and CS induced proteinuria remission providing renoprotection. The use of G-CSF every other day has resolved severe neutropenia episodes and therefore decreased the frequency of viral infections, contributing to a significant reduction of AKI episodes as well as hospitalization rate. Whether IgA nephropathy is genetically associated with cyclic neutropenia, or these two conditions simply coincide in this patient remains to be determined.

Glomerulonephritis (including vasculitides)

P2-365 - Native kidney disease in the Flemish pediatric population: results from the FCGG kidney biopsy registry

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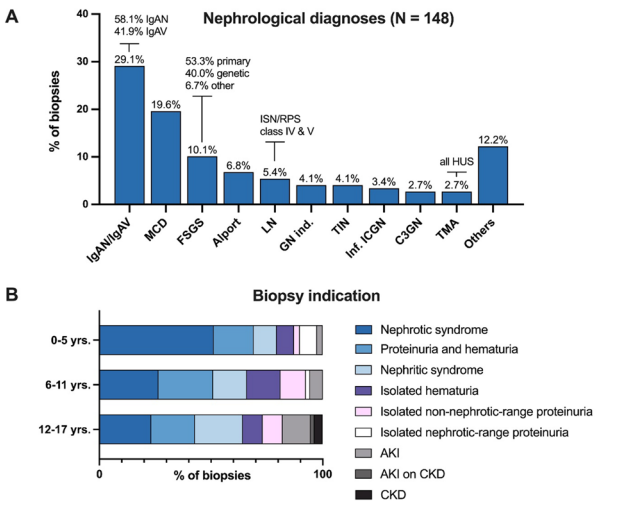
Background: The Flemish Collaborative Glomerulonephritis Group (FCGG) registry is a population-based kidney biopsy registry that has been including all pediatric native kidney biopsies performed in the Flemish population since 2017 (Northern part of Belgium, 6.5 million inhabitants).
Methods: From 2017 until 2020, 148 first pediatric (< 18 yrs.) native kidney biopsies from 15 nephrology centers were identified. Nephrological diagnoses, coded according to the ERA PRD coding system, are shown. Disease chronicity, summarized by the Mayo Clinic Chronicity Score (MCCS), was determined on 122 biopsies with > 5 glomeruli.
Results: Kidney biopsy rate was high (29.0 first biopsies per million children per year), median age was 10.0 yrs. (IQR, 5.8-14.7) and boys were predominant (56.1% males). In 100 biopsies (67.6%) at least 10 glomeruli were present and 140 biopsies (94.6%) showed a representative pathology result. Glomerular disease was most frequent, with IgA nephropathy/IgA vasculitis (43 biopsies, 29.1%) and minimal change disease (MCD, 29 biopsies, 19.6%) being the overall most frequent diagnoses (Fig. 1A). Children were most often biopsied because of nephrotic syndrome (31.8%), which was mainly caused by MCD and focal segmental glomerulosclerosis (FSGS, 55.3% and 25.5% of nephrotic patients, respectively). In the 0-5 yrs. age category, nephrotic etiologies were most frequent (Fig. 1B). In the 6-11 yrs. age category, nephritic etiologies and glomerular basement membrane abnormalities became more prevalent. In the 12-17 yrs. age category, biopsies were increasingly performed because of acute or chronic kidney disease, corresponding with higher frequencies of lupus nephritis, tubulointerstitial nephritis and thrombotic microangiopathy. Disease chronicity on kidney biopsies was generally low, although 27.3% of biopsies with FSGS showed moderate to severe chronic damage.
Conclusion: The completeness and granularity of collected histopathological data in FCGG is unique for a population-based registry and allows clinicopathological correlation, kidney biopsy quality control and estimation of disease chronicity on the population-level.



Abbreviations:
AKI: acute kidney injury; Alport: Alport syndrome; CKD: chronic kidney disease; C3GN: C3 glomerulonephritis; FSGS: focal segmental glomerulosclerosis; GN ind.: glomerulonephritis, histologically indeterminate; HUS: hemolytic uremic syndrome; IgAN: IgA nephropathy; IgAV: IgA vasculitis; ISN/RPS: International Society of Nephrology/Renal Pathology Society (classification of lupus nephritis); LN: lupus nephritis; MCD: minimal change disease; TIN: tubulointerstitial nephritis; TMA: thrombotic microangiopathy.

Glomerulonephritis (including vasculitides)

P2-366 - IgA nephropathy and juvenile idiopathic arthritis : 2 case reports

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Introduction: Renal manifestations are uncommon in juvenile idiopathic arthritis (JIA) and include a broad spectrum of glomerular and tubulointerstitial lesions. Although not totally understood, administration of nephrotoxic drugs and chronic systemic inflammation have been implicated in the pathogenesis of renal complications. IgA nephropathy is one of the most frequent primary glomerular diseases in adult patients with rheumatoid arthritis but has been occasionally reported in pediatric patients with JIA.
Methods: We report 2 pediatric patients with JIA, who presented acute glomerulonephritis compatible with IgA nephropathy.
Results: Two girls 12 and 15 years old were diagnosed with JIA since 5 and 2 years respectively. Both patients were treated with biological agent or methotrexate and the disease was in remission at the time of renal findings. The patients presented with microscopic hematuria and mild albuminuria. At the laboratory work-up, both patients had normal glomerular filtration rate, positive antinuclear antibodies and normal C3 and C4 levels. The rest of the immunological tests were normal. Both patients underwent kidney biopsy. Histopathological examination showed diffuse mesangial IgA deposits, mesangial and endocapillary hypercellularity associated with segmental glomerulosclerosis in both patients. These findings revealed the presence of IgA nephropathy with M1E1S1T0 score according to Oxford classification.
Conclusion: Renal involvement is common in childhood autoimmune diseases. IgA nephropathy has been rarely described in patients with JIA. Kidney biopsy is indicated in patients with JIA and combined hematuria and proteinuria in order to exclude JIA associated glomerulonephritis.

Glomerulonephritis (including vasculitides)

P2-367 - Rituximab treatment induced hypogammaglobulinemia in children with ANCA vasculitis and renal failure

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Background: Hypogammaglobulinemia following treatment of autoimmune disease with rituximab (RTX) has previously been described, however in pediatric patients, this phenomenon is rarely reported. In this observational study we evaluated immunoglobulin levels followed induction and maintenance treatment with RTX in children diagnosed with anti-neutrophil cytoplasm antibody (ANCA) associated vasculitis (AAV) admitted to Alberta Children's Hospital between 2015 and 2020.
Methods: A single center prospective study included consecutive children with AAV treated with RTX administered at 500 mg/m^2 twice with 2 weeks apart at induction followed by maintenance therapy 500 mg/m^2 q6 months were retrospectively identified. Demographic data, AAV phenotype and relevant laboratory results of blood and urine samples were documented. Hypogammaglobulinemia was defined as IgG<7 g/L=mild, IgG<5 g/L= moderate and IgG<2g/L =severe.
Results: A total of pediatric AAV patients, four girls, two boys were included; median age was 14.6 years (range 5- 17). Five had renal phenotype and one had mainly involvement of respiratory tract without renal involvement. All patients had normal IgG levels prior to treatment and were followed for 12-55 months. Children with a renal phenotype developed persisting hypogammaglobulinemia; one severe, three moderate and one mild. The patient without renal involvement was not affected. None of the patients had nephrotic range proteinuria or had severe infections. None received IVIG treatment. By the end of the follow-up period, only one patient recovered with a normal IgG level after renal transplantation.
Conclusion: Children with AAV and renal involvement appear to be at higher risk of developing hypogammaglobinemia with RTX treatment. However, risk for severe bacterial infections and immunoglobulin levels eventually recover. Observed hypogammaglobulinemia is unlikely to be related to proteinuria. More studies are needed to confirm that patients with AAV and renal failure are at higher risk for hypogammaglobulinemia.

Glomerulonephritis (including vasculitides)

P2-368 - Silent lupus nephritis: An indication for baseline renal biopsies in Systemic Lupus Erythematosus? Case series and a systematic review of the literature

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Introduction: Silent lupus nephritis (sLN) is defined as morphologic evidence of renal disease in systemic lupus erythematosus (SLE) patients without overt clinical renal manifestations. Current practice as to whether a baseline renal biopsy is indicated in SLE patients without overt signs of renal disease varies considerably among centers.
Objectives: To conduct a systematic review to evaluate the proportion of histologically confirmed cases of proliferative LN among children with sLN and to estimate the prevalence of sLN. In addition, we report three pediatric cases of sLN at initial presentation at our center.
Methods: Citations of pediatric and adult patients with sLN were retrieved using MEDLINE, Embase, CINAHL Plus, Scopus and Web of Science according to the PRISMA guidelines. Relevant publications from 1948 to 2020 with baseline biopsy results and renal histopathological classification available were included. Additionally, three sLN cases encountered in our center were also described.

Results: Thirty-three studies involving 504 patients (2-70 years) with sLN were included in the systematic review; of which 72 were <18 years of age. 29.2% of biopsies confirmed class III, class IV or class V LN. The proportion was similar in adults (28.1%). The three cases of sLN from our center were females with SLE; aged 9, 12 and 14 years. All patients underwent baseline renal biopsy to assist with treatment choices. LN Class III was demonstrated in two biopsies and LN Class II in the third.
Conclusion: This systematic review demonstrates that significant histologic LN findings are frequently found in children with SLE in the absence of overt signs of renal involvement. As such, baseline kidney biopsy in all newly diagnosed children with SLE may be justified. However, the clinical significance of sLN as well as the effect of treatment modification influenced by detection of this entity will require randomized prospective clinical research.

Glomerulonephritis (including vasculitides)

P2-370 - Anti-glomerular basement membrane disease: SARS-CoV-2 trigger or concealer?

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Anti-glomerular basement membrane disease (Anti-GBM), a rare autoimmune small-vessel vasculitis, causes rapidly progressive glomerulonephritis and acute pulmonary hemorrhage. Treatment in children is based on adult data; however, prognosis remains poor.
A 17-year-old boy, smoker (20cigarettes/day), healthy and fully vaccinated against SARS-CoV-2, presented to the emergency department with an 11-day history of dyspnea on mild exertion, thoracalgia, and blood-tinged sputum since D4. At presentation, respiratory distress, hypoxemia, and crackles were noticed. Blood analysis showed increased inflammatory markers and normal kidney function. Thoracic angio-CT-scan showed multiple micronodular opacities and excluded pulmonary embolism. PCR for SARS-CoV-2 was positive.
Hypoxemia worsened rapidly, refractory to mechanical ventilation and high-dose steroid-therapy, requiring extracorporeal membrane oxygenation for two weeks. Patient was discharged after fifty days, clinically improved; there were no further episodes of hemoptysis nor kidney function impairment.
Two months after discharge, he was re-admitted with a 5-day history of gross hematuria and progressive kidney injury. Despite oral high-dose steroid-therapy, kidney function continued deteriorating, and hemodialysis was started on D4. Anti-GBM-antibody levels were known on D5 (1139U/mL), kidney pathology showed crescentic glomerulonephritis (fibrocellular crescents in all glomeruli), and a diagnosis of anti-GBM was established. He was started on daily plasmapheresis, methylprednisolone bolus (3) followed by oral prednisolone, and cyclophosphamide. Two-weeks into treatment, after presenting desaturation during sleep and two hemoptysis, a bronchoscopy confirmed alveolar hemorrhage and anti-GBM-antibody levels remained elevated (659U/mL), and cyclophosphamide was switched to rituximab. At discharge, anti-GBM-antibody levels had decreased to near-normal values, pulmonary symptoms resolved, but no renal recovery was observed (expected for presentation severity), so regular hemodialysis was maintained.
An association between anti-GBM and COVID-19 has been hypothesized, since recent reports describe increased incidence of this condition during the pandemic. This case reports another example of this association, but the doubt if SARS-CoV-2 could have been the trigger or just an "innocent" bi-stander will probably remain.

Glomerulonephritis (including vasculitides)

P2-372 - The role of a step wise complement-mediated neutrophil activation via NETosis in the pathogenesis of C3 glomerulopathy

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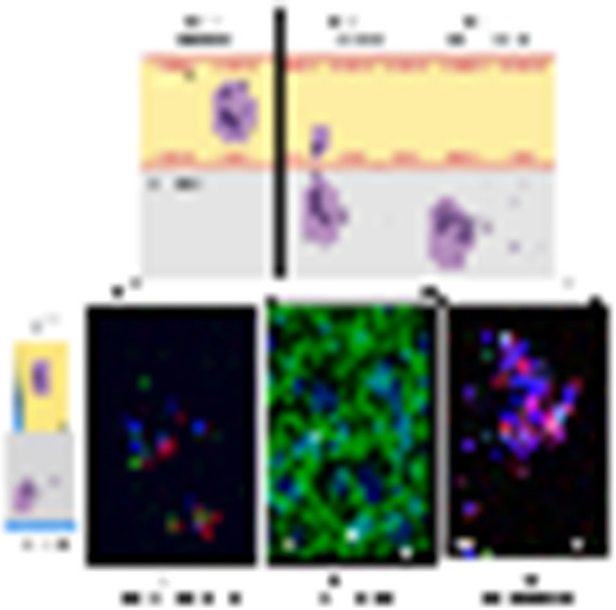
C3 Glomerulopathy (C3G) is a rare chronic disease that affects the functional unit of the kidney, the glomerulus. It is characterized by protein deposits in the extravascular tissue of the kidney which leads to inflammation, tissue damage, and eventually End Stage Renal Disease requiring transplantation. Although we know C3G is a complement-driven disease there is a gap in the pathogenetic cascade from complement activation (intravascular space) to inflammation and deposition in the glomeruli (extravascular space). Recently, C3G patients were found to have significant amounts of polymorphonuclear neutrophils (PMNs) infiltrating their glomeruli, suggesting a so far underappreciated aspect of C3G pathogenesis.
Given the chronic complement dysregulation found in C3G patients, we investigated the complement-induced responses of PMNs using a transwell model allowing for different environments resembling the kidney intravascular space (top well; serum containing) versus extravascular space (bottom well; serum-free conditions). Complement stimulated PMNs in the top well were allowed to transmigrate to the bottom well where they were monitored for the formation of Neutrophil Extracellular Traps (NETs) via immunofluorescence and SYTOX assay.
We found a stepwise PMN activation with upregulation of PMN priming markers, including CD11b, myeloperoxidase (MPO), and citrullinated Histone 3 (CitH3) but not complete NETosis (intact nuclear membrane) in serum containing conditions. Only once these PMNs transmigrated to serum-free conditions, PMNs completed the process of NETosis. Complement stimulated PMNs were also found to adhere more strongly to a monolayer of endothelial cells when compared to unstimulated controls. Our results were confirmed using C3G patient PMNs kept in complement active (autologous) serum.
These findings not only advance our understanding of C3G pathogenesis but can also significantly change the management of C3G patients through more specific monitoring and treatment strategies that target complement activation, PMN activation, or both, for whom currently, specific treatment is lacking, and patient outcomes are poor.



Glomerulonephritis (including vasculitides)

P2-374 - Pediatric anti-glomerular basement membrane disease: five case reports

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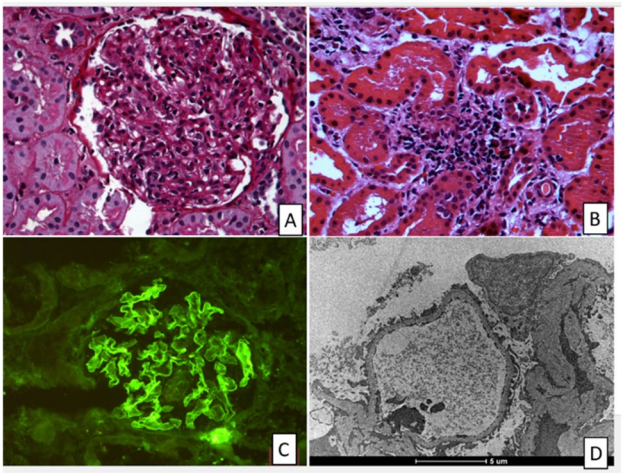
Background: Anti-glomerular basement membrane (anti-GBM) disease is a rarely entity in the pediatric population characterized by rapidly progressive glomerulonephritis (RPGN), often without pulmonary involvement. Although rare in children, its possibility must be considered in the differential diagnosis of acute renal failure and glomerulonephritis.
Cases–Diagnosis/Treatment: We described five cases of pediatric patients with the diagnosis of anti-GBM disease based on kidney biopsy and on the clinical presentation of RPGN, with or without pulmonary involvement. All patients were adolescents and the majority were male. In all cases there was a report of cough or milder flu-like symptoms. One patient demonstrated alveolar hemorrhage and another presented pneumonia. Proteinuria nephrotic or non-nephrotic was a common finding in all patients and most of them had hematuria. All patients had a clinical presentation as RPGN. The degree of renal dysfunction was more severe in younger patients, who presented positive FAN. Only one of the kidney biopsies did not show crescents and this patient had better renal function and lower percentage of fibrosis. All biopsies were positive for IgG with linear deposit on GBM on immunofluorescence. Lambda deposits were positive in all cases, three had few C3 deposits and Kappa was negative only in one case. Two patients had the presence of anti-GBM antibodies confirmed. In another two, the anti-GBM antibody measurement was negative, and in one, the information was not available. Four patients were treated with corticosteroids and cyclophosphamide. Two patients underwent plasmapheresis, however, they did not recover renal function. The patient without crescents on kidney biopsy did not progress to complete loss of kidney function. The others required renal replacement therapy and one patient died.
Conclusion: We do believe that any case of anti-GBM should be described in order to better understand this rare pediatric disease.
A) PAS stain B) H&E C) Immunofluorescence D) Transmission Electron Microscopy



Glomerulonephritis (including vasculitides)

P2-375 - Using red cell distributon width index as an alternative predictor for lupus nephritis activity in Dr. Soetomo Hospital Surabaya Indonesia

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Background: Management of Systemic Lupus Erythematosus (SLE) requires continuous monitoring for its disease activity since SLE is an autoimmune disorder that manifests as a chronic inflammatory disorder with multisystem involvement. Lupus nephritis is found in nearly 50% patients with pediatric-onset SLE. The SLE Disease Activity Index (SLEDAI) and multiple serum markers, anti-dsDNA and antinuclear antibodies as part of SLEDAI scoring itself, have been extensively used for more than 20 years in evaluation of SLE inflammatory status. However, these tests are expensive and inconvenient. Recently, increased Red Distribution Width (RDW) has been linked to systemic inflammation in

patients. Therefore, we aimed to analyze the correlation between RDW and SLEDAI as predictor for pediatric Lupus Nephritis disease activity.
Methods: A cross-sectional study involving 47 children diagnosed with lupus nephritis in the Pediatric Ward at Dr. Soetomo Hospital was conducted in March 2020-May 2021. Data of age, gender, RDW value and SLEDAI score for each patient at initial diagnosis were collected from medical records. RDW values by flow cytometry were divided into 2 criteria (according to age): normal and increased; while SLEDAI scores were divided into 2 groups: mild to moderate (score 0-12) and severe (score ≥13). The correlation between RDW and SLEDAI scores for SLE disease activity was analyzed using Kappa and McNemar tests ($p<0.05$).
Results: Most subjects were within the age groups of 11-18 years (51.1%) and 6-10 years (48.9%) with male:female ratio of 1.04:1. Severe SLEDAI score was found in 26 (55.3%) subjects and 37 (78.7%) subjects had increased RDW value. Increased RDW values were not significantly correlated with severe SLEDAI score ($\kappa=0.048$, $p=0.703$).
Conclusion: Our findings suggest that baseline RDW is a readily available parameter but may not be able to represent the overall activity of lupus nephritis.
Keywords: Lupus Nephritis, RDW, SLEDAI, predictor, disease activity

Glomerulonephritis (including vasculitides)

P2-376 - Characteristics and outcomes of C3 glomerulopathy in children: a single-center experience

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Background: C3 glomerulopathy (C3G) is a rare complement-mediated kidney disease characterized by dominant glomerular staining for C3 by immunofluorescence and encompasses C3 glomerulonephritis (C3GN) and dense deposit disease (DDD). Data regarding clinical course and long-term outcome in children with C3G is still scarce. The aim of the study was to investigate clinical and histopathological characteristics and outcomes in children with C3G.
Methods: We conducted retrospective study of 16 (7M/9F) children with C3G with median follow-up of 2.8 (IQR: 1.8; 5.6) years. All children were treated with immunosuppressive therapy (IST) including mycophenolate mofetil, cyclosporin A, tacrolimus, cyclophosphamide iv or rituximab.
Results: Among 16 children with C3G C3GN was found in 10 and DDD in 6 patients. Median age at onset of C3G was 11.5 (6.8; 14.5) years. All patients presented with steroid-resistant nephrotic syndrome (SRNS) with hematuria and hypertension. Light microscopy revealed MPGN in 9 (56.3%) children, FSGS in 6 (37.5%) subjects and crescentic GN in 1 (6.2%) case. At the last follow-up complete (CR) and partial remission (PR) of C3GP were obtained in 1 (6.2%) and 6 (37.5%) patients, respectively. There was no effect of IST in 9 (56.3%) children. Median eGFR at the 1st and the last follow-up were different significantly: 86.0 (64.3; 108.3) vs. 74.5 (55.3; 85.8) ml/min/1.73 m^2 ($P<0.01$). At the end of follow-up, CKD-1 was found in 2 (12.5%) patients with C3GN; CKD-2 in 9 (56.3%) children with C3GN (n=6) and DDD (n=3); CKD-3 in 3 (18.8%) subjects with C3GN (n=2) and DDD (n=1); CKD-4 in 2 (12.5%) cases with DDD.
Conclusions: All children with C3G presented with SRNS with hematuria and hypertension. CR and PR were induced in 43.7% of patients, while progression to CKD2-4 was found in 87.5% of children with C3G. Effective anti-complement therapy is needed to prevent progression of C3G to CKD.

Glomerulonephritis (including vasculitides)

P2-378 - Utilizing pharmacokinetic studies to optimize therapy in a child with C3 glomerulonephritis and nephrotic syndrome – a precision medicine approach

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Introduction: C3 glomerulonephritis (C3GN) is caused by complement alternative pathway dysregulation, has no definitive treatment and is characterized by progression to kidney failure. Terminal complement blockade has successfully been used, especially in patients with elevated C5b-9 levels.
Case Description: We describe a 6-year-old boy with C3GN, who presented with nephrotic syndrome, severe hypertension (4 antihypertensive medications) and acute kidney injury. Complement C3 level was 0.12 g/L (normal 0.8-1.5) with pos C3NeF and elevated C5b-9 levels (2135, normal <239ng/ml). Despite 6 months of treatment with steroid and MMF, he had ongoing nephrotic syndrome and worsening kidney function and was commenced on Eculizumab (standard dosing). Despite a further 6 months of therapy, he had persistent severe hypertension, nephrotic syndrome requiring weekly albumin/furosemide infusions and worsening kidney function. Complement C3 levels remained low with elevated C5b-9 levels, suggesting sub-optimal terminal complement inhibition due to urinary loss. We confirmed sub-therapeutic plasma concentrations of eculizumab as free plasma eculizumab levels were low on day 7 (9, normal >99 ug/ml) and undetectable on days 10 and 14 post-infusion. Eculizumab was detected in urine, indicating urinary loss. Eculizumab frequency was subsequently increased to weekly with MPA-AUC guided adjustment of MMF dosing. Since then, his kidney function, C5b-9 levels (297ng/ml) and nephrotic syndrome improved significantly, leading to the discontinuation of albumin/furosemide and anti-hypertensive medications. With the improved kidney function, we were also able to initiate treatment with an ACE inhibitor. Despite very high doses of Cellcept™ and not being a rapid metabolizer, the patient has not achieved target MPA-AUC between 30-60 mg x hour/L. Due to several viral infections in the last 9 months, we have not optimized his dose further. Eculizumab and MMF have been well tolerated.
Discussion: Pharmacokinetic studies should be considered to individualize treatment in C3GN patients with ongoing proteinuria who failed to respond to standard dosing.

Glomerulonephritis (including vasculitides)

P2-379 - Treatment of IgA vasculitis with biopsy proven nephritis to improve midterm outcome remains unclear- a multicentre study of 1175 children

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Objectives: IgA Vasculitis Nephritis (IgAVN) is self-limiting in a large majority of cases but a proportion of affected children develop proteinuria and rarely worsening kidney function. International guidelines recommend treatment with angiotensin converting enzyme (ACE) inhibitors and corticosteroids in severe disease, whereas benefit of further immunosuppressive treatment is debated.
The aim of our study is to define treatment modalities that have an effect on outcome in a large cohort of children with biopsy-proven IgAVN.
Methods: Data were collected through a retrospective international survey from December 2020 to August 2021. Anonymised demographic and clinical data (including renal outcome data) were collected from children (0-18 years of age) with typical symptoms of IgA vasculitis, kidney biopsy proven IgAVN and a minimal follow up of 12 months.
Results: Data from 1160 patients were collected from 41 international paediatric nephrology centres. Median age at renal biopsy was 8.3 years, 43 % female, median duration of follow up 3.7 years. 3.5% of the patients (3.5 %) had an estimated glomerular filtration rate (eGFR) below 30 ml/min/1.73m^2 and 2.6 % needed renal replacement therapy at presentation, 95.2% had proteinuria, 61.8% within nephrotic range. 80.2% received treatment with ACE-inhibitors, 42.3% had intravenous steroids and long term oral steroid treatment and 38.4% oral steroid treatment alone. Additional drugs used included Mycophenolate mofetil (13.1%), Azathioprine (12.1%), Cyclophosphamide (17.1%), Calcineurin-inhibitors (10%), intravenous Immunoglobulins (0.6%), Rituximab (1%) and Anticoagulants (10.3%).
No benefit of any treatment given on eGFR or proteinuria in the medium term could be detected. Statistical analyses were limited by low numbers in the different subgroups.
Conclusion: This cohort is the largest study on children with biopsy proven IgAVN. Most centres followed the current treatment recommendations for initial treatment, but additional treatment is variable. Potential benefits of immunosuppression on medium term outcome remains unclear.

Glomerulonephritis (including vasculitides)

P2-380 - Clinical manifestations and pathological correlation of Immunoglobulin A Nephropathy: Short-term outcomes in children

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Background: IgA nephropathy in children has various clinical manifestations from asymptomatic to severe symptoms that can cause chronic kidney disease. Kidney biopsy is a gold standard for diagnosis by using Oxford classification 2016 with few studies about the correlation between clinical and pathology manifestations. This study aims to find the correlation between the presenting of symptoms and the severity of pathological findings at the time of diagnosis and during short-term follow-up.
Material and method: In this retrospective cohort study, 47 pediatric patients who underwent renal biopsy from 2010 to 2021 in Thailand, were included. Oxford classification 2016 has been used to score patients' pathology. Univariate and multivariate associations have been used for correlation between clinical and pathologic parameters.
Results: The most common clinical manifestations were microscopic hematuria and proteinuria. There were 68% of children with mesangial hypercellularity (M1), 42% with segmental glomerulosclerosis (S1), 25% with moderate to severe crescent (C1/C2), 23% with endocapillary hypercellularity (E1), and 14% with moderate to a severe tubular atrophy/interstitial fibrosis (T1/T2). Microscopic hematuria was strongly associated with mesangial hypercellularity (M1) OR 7.14 (95%CI 1.83 – 27.88, p-value 0.005) and hypertension was strongly associated with segmental glomerulosclerosis (S1) adjusted OR 7.87 (95%CI 1.65 – 37.59 P-value 0.01).There was no change of serum creatinine and estimated glomerular filtration rate at 6,12 and 24 months. Intensive treatment was used more in the patients with tubular atrophy/interstitial fibrosis lesion on renal biopsy than other lesions from MEST-C scores OR 4.98 (95%CI 1.17-21.24, p-value 0.03). Furthermore, pulse methylprednisolone and cyclophosphamide were used in patients with crescentic lesions significantly than other lesions with OR 15.5 (95%CI 3.16- 75.93, p-value 0.001) and OR 5.75 (95%CI 1.31-25.29, p-value 0.021), respectively.
Conclusion: Tubular atrophy/interstitial fibrosis and crescent lesions were correlated to intensive treatment in short-term outcomes.

Glomerulonephritis (including vasculitides)

P2-382 - Efficacy of new combination therapy with prednisolone, mizoribine, and lisinopril for severe childhood IgA Nephropathy.

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Objectives: Angiotensin-converting enzyme inhibitors such as lisinopril have been widely used for childhood IgAN since the 2000s. In our previous randomized control trial, combination treatment including prednisolone (PSL) and mizoribine (MZB) with warfarin and dipyridamole may be better for severe childhood IgAN than the combination treatment including PSL and MZB without warfarin nor dipyridamole from the point of proteinuria remission. However, we should consider new combination therapy such as PSL, MZB, and lisinopril considering warfarin nephropathy and shortening the duration of PSL use.
Method: This cohort study included 84 patients with severe IgAN enrolled among 546 pediatric IgAN between 1977 and 2017 and divided into 2 groups, 70 patients who were treated with previous combination therapy or 14 patients with new combination therapy. A 1:1 propensity score matching was performed to account for between-group differences and 12 matched pairs were obtained.

Results: In the comparison of the 12 matched pairs, the Kaplan-Meier analysis of proteinuria remission (uP/Cr < 0.15) showed that there was a significant difference in proteinuria remission rate between the groups (100% vs. 59.3% at 3 years, p=0.001). Furthermore, the patients with new treatment achieved significantly faster proteinuria remission than those with previous treatment (Median 2.4 vs 12 months, p=0.04). The median duration of PSL use was significantly shorter in the new treatment group (13 vs. 24 months, p< 0.0001). The median observation period was 4.9 and 4.5 years, and the percentage of patients with normal urine at the latest observation was significantly higher in the new treatment group (66.7% vs. 25.0%, p=0.04).
Conclusion: We confirmed the usefulness of a new combination treatment with PSL, MZB, and lisinopril for severe childhood IgAN in achieving early proteinuria remission and shortening PSL use. Further investigations with the larger-scale and long-term outcomes will be needed.

Glomerulonephritis (including vasculitides)

P2-383 - Peripheral blood CD19+CD27+CD38+ cells in childhood-onset collagen diseases with kidney involvement

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Introduction: $CD38^+$ cells that produce autoantibodies have an important role in chronic inflammation. Benfaremo et al. reported that $CD38^+$ cells are potential therapeutic targets in autoimmune diseases such as systemic lupus erythematosus (SLE) and primary Sjögren's syndrome (pSS). By contrast, there have been few reports on the relationship between $CD38^+$ cells and kidney involvement associated with autoimmune diseases.
Materials & Methods: Peripheral blood $CD19^+CD27^+CD38^+$ cell counts were performed in seven children with childhood-onset collagen diseases (SLE: two cases, pSS: four cases, sarcoidosis: one case) treated at the University of the Ryukyus Hospital between 2018 and 2021. Flow cytometry data analysis was performed to identify B-cell subsets of peripheral blood mononuclear cells via their expression of cell surface markers (CD19, CD24, IgD, CD27, CD38). We compared the percentage of $CD38^+$ cells in patients with SLE and pSS with or without kidney involvement.
Results: The percentage of $CD19^+CD27^+CD38^+$ cells increased in one case of lupus nephritis class IV (ISN/RPS classification) and one case of pSS with nephrotic syndrome (35.3% and 22.9%, respectively). In lupus nephritis class IV patients, the percentage of $CD19^+CD27^+CD38^+$ cells decreased to 1.3% after initial treatment, and in pSS patients with nephrotic syndrome, the percentage decreased to 7.0% after initial treatment and to 2.0% after remission. However, one case of lupus nephritis class V without urinalysis abnormalities, three cases of pSS without kidney involvement, and one case of sarcoidosis with kidney dysfunction refractory to treatment due to tubulointerstitial nephritis showed no increase in the percentage of $CD19^+CD27^+CD38^+$ cells.
Conclusion: $CD19^+CD27^+CD38^+$ cells might be associated with kidney involvement in childhood-onset SLE and pSS, which are autoimmune diseases. The decrease in $CD19^+CD27^+CD38^+$ cells after treatment may help determine treatment efficacy and CD38 might be a therapeutic target in childhood-onset collagen diseases with kidney involvement.

Glomerulonephritis (including vasculitides)

P2-384 - Clinicopathological profile of pediatric lupus nephritis : data from the lupus nephritic clinic of a tertiary care hospital in Eastern India

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Background: Childhood lupus can involve multiple organs with kidney being the most important organ determining long term prognosis.
Aims and Objectives: To study the clinicopathological profile of pediatric lupus nephritis (LN) and assess treatment response / outcome.
Material and methods: Cross sectional observational study including children with biopsy proven LN.
Results: Total number= 60; female: male= 4:1; median age at diagnosis: 11 (IQR: 9 to 12) years. Median duration of follow up was 5.6 (IQR: 1.8 to 6.8). Most common extra-renal manifestations was mucocutaneous (58%) followed by hematological (47%). Fever (92%), rash (92%) and oedema (82%) were the commonest presentations. Most common biochemical parameter detected was proteinuria; Median 1.4 (IQR 0.6 to 2.3) gm. At presentation Anti Nuclear Antibody was positive in all; C3 was low in 92% and C4 in 87%. Anti-phospholipid antibody was positive in 18%. On biopsy Class IV Lupus Nephritis was most common (70%; n=42 +3 had class IV + V), Isolated Class V seen in 12% (n=7) and Class VI seen in one child. All children received steroids (pulse/oral). Mycophenolate Mofetil was given as induction agent in 72%. Rituximab was used in 17% (n = 10) as a rescue agent and Tacrolimus was used in 1 child. Complete Response (CR) was seen in 72% (n=43) at 12 months. Median time to remission: 6 (IQR: 4 to 6.25) months. Incidence of Flares: 0.16/person year. Median time to first flare after achieving complete remission: 19 (IQR: 15 to 22) months. Outcomes at last follow up: CR 73%, partial responders 20 % and non-responders 7 %. Mortality rate: 8 % (n=5; 2 had ESRD, and all died from serious infections).
Conclusion: Childhood LN remains a challenge with 8% mortality and over a quarter of children remaining partial or non responder at last follow up.

Glomerulonephritis (including vasculitides)

P2-385 - Development of a coated mini-tablet formulation for iptacopan and evaluating the acceptability, swallowability and palatability of multiple mini-tablets in young children

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Background: Iptacopan (LNP023) is an orally administered complement alternative pathway Factor B inhibitor under development in adults and children for the treatment of complement-mediated kidney diseases. Physicochemical properties of the compound create challenges for liquid formulation development and necessitate alternative

strategies. Coated mini-tablets represent an innovative approach to this challenge and have previously been demonstrated to be acceptable to infants and children and allow flexible dosing (Klingmann, *J Pediatr* 2013).

Methods: The aim of this mini-tablet formulation study is to investigate the acceptability, swallowability and palatability of a high quantity of 2-mm diameter coated placebo mini-tablets compared with a low quantity of 2.5-mm coated placebo mini-tablets in children aged 1 month to 6 years. This will allow selection of the optimal mini-tablet size for further development. Participants comprise 360 children (72 per age group: 36 per age group and dosing arm) residing/attending outpatient clinics at University Children's Hospital Düsseldorf. The study is performed in five consecutive age groups (4–6 years, 2–<4 years, 1–<2 years, 6–<12 months, 1–<6 months) each with two randomised parallel arms receiving a high or low number of mini-tablets. Within each arm, the 2-mm and 2.5-mm mini-tablets will be compared in a randomised cross-over fashion. Acceptability, assessed by five scoring criteria for both swallowability and palatability, will be derived from a binary outcome score. Acceptability rates will be compared between the two regimens (high quantity of 2-mm vs. low quantity of 2.5-mm mini-tablets). Corresponding two-sided 90% confidence intervals will be calculated for the averaged difference of acceptability rates.

Results and Conclusions: Over 185 children have been recruited since February-2022. No adverse events have occurred to date. Full results of the study will be presented at the meeting. Coated mini-tablets are a suitable and promising innovative alternative formulation for use in younger children.

Glomerulonephritis (including vasculitides)

P2-387 - First nationwide survey of severe pediatric Henoch-Schönlein purpura nephritis in Japan -Age at kidney biopsy and NS persisting for more than 3 months are predictors of kidney prognosis-

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Introduction: In children with Henoch–Schönlein purpura nephritis (HSPN), nephrotic syndrome (NS) persistence for ≥3 months has been reported to be a poor prognosis. This nationwide cohort study of severe pediatric HSPN in Japan investigated prognostic factors for HSPN.

Material & Methods: Overall, 476 questionnaires were collected from 98 institutions (response rate, 89%) for children aged 1–15 years with biopsy-proven HSPN between 2013 and 2015. Included patients received prednisolone plus immunosuppressants and had >2 years of follow-up records. Poor prognosis comprised kidney dysfunction (estimated glomerular filtration rate <80 mL/min/1.73 m^2) or residual proteinuria (urinary total protein/creatinine ≥0.2 g/g creatinine) at the last observation. Patients were divided into three groups: NS (albumin <3.0 g/dL) persistence for ≥3 months (NS ≥3 m), NS persistence for <3 months (NS <3 m), and non-NS.

Results: We analyzed 273 patients (median observation period, 69 months; interquartile range, 52–81). NS ≥3 m, NS <3 m, and non-NS groups comprised 46, 59, and 168 cases, respectively (21, 38, and 98 boys); median ages at kidney biopsy (KBx) were 6.7, 7.0, and 7.3 years; kidney dysfunction at KBx was observed in seven, 11, and eight patients; 14, four, and 22 patients had poor prognosis. Kidney pathology showed International Study of Kidney Disease in Children (ISKDC) grade 2–3a/3b–5 in 15 and 31 patients (NS ≥3 m), 24 and 31 patients (NS <3 m), and 83 and 83 patients (non-NS). Age (odds ratio, 1.014 [confidence interval, 1.004–1.024]) and NS ≥3 m (versus non-NS) (odds ratio, 3.537 [confidence interval, 1.507–8.298]) constituted risk factors for poor prognosis after adjustment for kidney dysfunction and kidney histology.

Discussion: Patients with NS persistence for ≥3 months exhibited poor prognosis and may require risk-based management. ISKDC classification findings were not associated with prognosis. Relationships with other pathological classifications (e.g., Oxford) require further investigation.

Glomerulonephritis (including vasculitides)

P2-388 - Kidney outcome in an international cohort of children and adolescents with lupus nephritis

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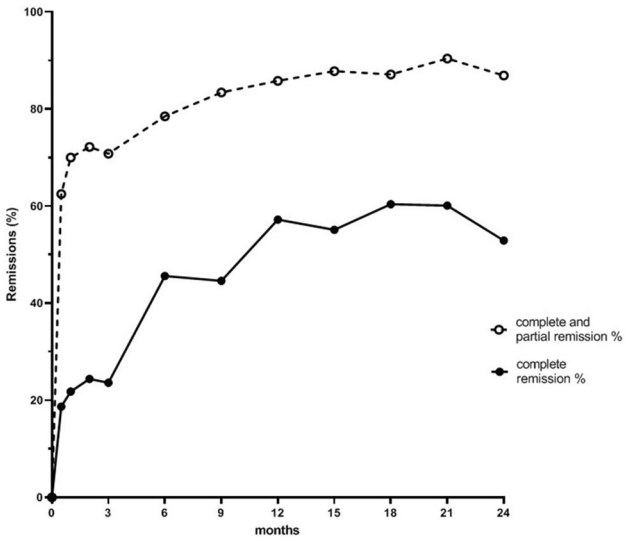
Introduction: Children with lupus nephritis (LN) have higher risk for end stage renal disease and higher mortality compared with age-matched healthy children. We present kidney outcome of an international cohort of children with LN.

Material and methods: 382 patients (≤18 years old) with LN class ≥ III diagnosed and treated in the last 10 years in 23 international centers were studied up to 24 months of follow-up. We defined complete remission as urine-protein-creatinine ratio ≤ 0.2 mg/mg and eGFR ≥90 ml/min/1.73m2 or serum creatinine increase less than 15%. Partial remission was defined as urine-protein-creatinine ratio < 2 mg/mg or a 50% reduction if UPCR ≥ 2 at baseline and eGFR ≥90 ml/min/1.73m2 or serum creatinine increase less than 25%. Stable remission was considered as the persistence of complete remission from 6th months to 24th months of follow up and assessed in a subgroup of 351 patients.

Results: 57% and 34% of patients achieved complete and partial remission at 24-month follow-up, respectively (Figure 1). Only 25.4% maintained stable remission. The reasons why patients didn't achieved stable remission were eGFR < 90 ml/min/1.73m2 in 16.8%-30.5% of cases, increased serum creatinine in 6.8%-13.1% and urine-protein-creatinine ratio > 0.2 mg/mg in 29.3%-45.6%. Patients with biopsy class III achieved complete remission more often than other biopsy classes. Complement 3, serum creatinine, urea and biopsy class at diagnosis were predictive parameters of stable renal remission.

No difference in achieving stable remission was found between children who received mycophenolate or cyclophosphamide as induction treatment.

Conclusions: In our cohort the rate of stable complete remission in patients with LN is still low. Severe kidney involvement at diagnosis was the most important risk factor for not achieving stable remission while no difference were found between induction treatments. Randomized treatment trials in children with LN are needed to improve kidney outcome.



Glomerulonephritis (including vasculitides)

P2-389 - A girl with lupus nephritis complicated with infectious pneumonia

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Introduction: The incidence of infectious pneumonia was approximately 30% in patients with systemic lupus erythematosus (SLE). It is difficult to distinguish between infectious pneumonia and interstitial lung disease associated with systemic lupus erythematosus (SLE).
Materials and Methods: The clinical data of a girl with SLE and lupus nephritis (LN), 13 years old, was collected. She was admitted for "chest pain for half a day". Her chest high-resolution computed tomography (HRCT) and a lung biopsy were performed. Her metagenomic next-generation sequencing (mNGS) of bronchoalveolar lavage fluid (BLAF) were also performed.
Results: The patient's renal pathology was consistent with LN of Class IV (A/C). Her SLEDAI-2000 score was 18 points. Her chest HRCT revealed multiple patchy nodular increased density shadows in the right lung. Her right lung biopsy pathology showed fibrin exudates and neutrophils in alveolar space. The copies of DNA of mycoplasma pneumoniae in BLAF were 3.97×10^4. Her mNGS of BLAF showed that the number of sequences of nocardia was 5335, mycoplasma pneumoniae 6 and pneumocystis jirovecii 2. She was diagnosed with LN complicated with infectious pneumonia, who was treated with cefoperazone sodium sulbactam sodium, ceftriaxone, compound sulfamethoxazole, azithromycin and fluconazole. Her symptoms improved with the above treatments for two months. After one month of follow-up, her pneumonia was cured and SLEDAI-2000 score was decreased to 8 points.
Conclusions: Both lung biopsy pathology examination and mNGS of BLAF can distinguish between infectious pneumonia and interstitial lung disease associated with SLE.
Keywords: lupus nephritis, pneumonia, child, lung biopsy, metagenomic next-generation sequencing

Glomerulonephritis (including vasculitides)

P2-390 - Clinical and pathological features in IgA Nephropathy Patients with repeated renal Biopsy

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Objective: To investigate the clinical and pathological features of IgA nephropathy (IgAN) in pediatric patients underwent repeated renal biopsy
Methods: A total of 26 IgAN pediatric patients between 2 to 18 years old who underwent repeated renal biopsy in the First Affiliated Hospital of Sun Yat-sen University from 2003 to 2020 were collected.
Results: (1) General information and clinical indicators: repeat renal biopsy was performed in 21 males and 5 females. There were mainly three indications for repeated renal biopsy as following: evaluation for the efficacy of immunosuppressive therapy (22/26); Renal function deterioration (1/26); use of calcineurin inhibitors for more than 2 years (1/26) and increased proteinuria (2/26). The median interval between the two renal biopsies was 8 months.84% patients were administered with Methylprednisolone and(or) cyclophosphamide pulse therapy. The patients mostly had 24-hour quantitative urine protein (24h TP) positive continuously , increased 24h TP or serum creatinine within 3 months.(2) Pathological indexes: due to > 80% of the enrolled patients were evaluated for immunosuppressive therapy, the proportion with S/T , were significantly decreased in repeated renal biopsy. The time interval was not long enough to observed changes of chronic lesions, which were not so significant on repeated renal biopsy. (3) For patients with repeated renal biopsy due to decreased renal function or elevated proteinuria, immunosuppressive therapy was enhanced after the second renal biopsy compared with the first renal biopsy. (4) Patients underwent repeated renal biopsy did not had increased risk of complications, such as bleeding or infection etc.
Conclusion: repeated renal biopsy is relatively safe and it can be considered if serum creatinine increased in a short period or 24h TP is not in remission continuously as well as for efficacy-evaluation for immunosuppressive therapy. Methylprednisolone and cyclophosphamide therapy made benefit in children by reducing acute lesions in pediatric patients with IgAN

Glomerulonephritis (including vasculitides)

P2-392 - Macrophage colony-stimulating factor: a novel biomarker for pediatric lupus nephritis?

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Objectives: Overexpress of monocyte/macrophage-associated cytokines are increasingly recognized in lupus nephritis (LN). However, the intrinsic connection between serum M-CSF (sM-CSF) and pediatric LN remains to be clarified. Here, we explored clinical values of sM-CSF for monitoring of disease activity in children with LN.

Methods: 116 children with LN, who were hospitalized in the Pediatric Nephrology and Rheumatology Department of the First Affiliated Hospital, Sun Yat-sen University from September, 2014 to December, 2019 were enrolled in the case group in this retrospective study. Another 22 healthy children were enrolled as the control group. Enzyme linked immunosorbent assay was used to measure sM-CSF levels, and receiver operating characteristic (ROC) curve was used to analyze the value of sM-CSF and anti-dsDNA antibody levels in predicting LN disease activity. Spearman correlation analysis was performed to study the correlation of the sM-CSF levels with their laboratory indexes.
Results: The level of sM-CSF was significantly increased in the LN group rather than the control group. The LN group was classified into mild activity group (n=62) and moderate or severe activity group (n=54) according to SLEDAI-2000 score. As shown, moderate or severe activity group had higher levels of sM-CSF. The ROC curve analysis showed that the combination of sM-CSF and anti-dsDNA antibody had larger area under the ROC curve of 0.821 (95%*CI*: 0.741~0.901) to predict moderate and severe activity in children with LN rather than sM-CSF or anti-dsDNA alone. Correlation analysis showed that sM-CSF was positively correlated with anti-dsDNA antibody, anti-nuclear antibody, serum IgG and SLEDAI score, and negatively correlated with complement C3 and C4.
Conclusions: The level of sM-CSF was increased in children with LN, which was related with LN disease activity. M-CSF may be considered as a potential and promising marker to evaluate kidney disease activity in children with LN.

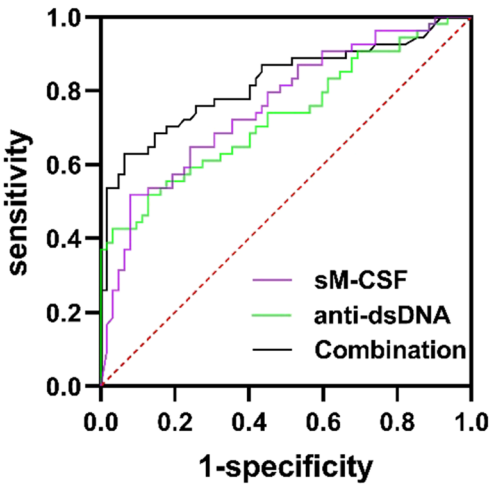

Fig.1 The ROC curve of serum M-CSF and anti-dsDNA antibody levels to predict LN disease activity

Glomerulonephritis (including vasculitides)

P2-393 - Hhyperuricemia is correlated with the progression of IgA nephropathy in children

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Background and aim: Immunoglobulin A nephropathy (IgAN) is the most common forms of primary glomerulonephritis in children. We aim to explore potential biomarkers and risk factors in IgAN children by metabolomic study.
Methods and results: Untargeted metabolomics analysis were performed on serum samples derived from IgAN children before and after treatments and controls. To further verify the role of hyperuricemia in IgAN children, a retrospectively study was conducted on the clinical and pathological data of IgAN children in past 15 years. The results of serum metabolites study showed that the levels of serum xanthosine (the precursor substance of serum uric acid (SUA)) were closely related to outcome of IgAN, and KEGG analyses showed that differential metabolites were significantly enriched in purine metabolism. Furthermore, the retrospectively analyses of 252 IgAN children also showed that IgAN children with hyperuricemia have poor renal function and worse renal pathology. Multivariate logistic regression analysis showed that body mass index, serum creatinine, low eGFR, Lee's grade III and crescents were risk factors of hyperuricemia in IgAN children. Multiple linear regression analysis found that high level of SUA was the risk factor affecting the progression of IgAN children.
Conclusions: We perform a dynamic metabolomics study for the first time to reveal that the level of SUA is closely related to the progression of IgAN children. Then the retrospective analyses also confirm that hyperuricemia is the risk factor for the poor renal outcome. Combined administration of urate-lowering therapy may help delay the progression of IgAN in children.
Keywords: immunoglobulin A Nephropathy; metabonomics; hyperuricemia; children; progression

Glomerulonephritis (including vasculitides)

P2-394 - Uric acid promote renal fibrosis in children with IgA nephropathy via PI3K-Akt-mTOR signaling pathway

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Aim: Hyperuricemia is correlated with the progression of Immunoglobulin A nephropathy (IgAN) in children. We aim to explore the mechanism of uric acid promoting renal fibrosis in Children with IgAN.
Methods: The 173 IgAN children diagnosed in the Department of Pediatric Nephrology and Rheumatology of the First Affiliated Hospital of Sun Yat-sen University from Jan. 2006 to Dec. 2021 were included and divided into hyperuricemia group (n=53) and non-hyperuricemia group (n= 120). The clinical and pathological correlations of the two groups were analyzed and the Kaplan-meier analysis were performed. The expression levels of p-RPS6、α-SMA and E-cadherin in kidney samples (22 in hyperuricemia group and 22 in non-hyperuricemia group) were detected by immunohistochemistry.
Results: The Kaplan-meier analysis showed that the cumulative renal survival rate was significant decreased in IgAN children with hyperuricemia (P<0.05). Compared to the non-hyperuricemia group, the expression levels of p-RPS6 and α-SMA were significantly higher and the levels of E-cadherin were significantly lower in hyperuricemia group (all P<0.01). The level of eGFR was negatively correlated with the expression level of p-RPS6 in renal sample of children with IgAN (r=-0.526, P<0.01). The expression levels of p-RPS6 (r=0.381, P<0.05) and α-SMA (r=0.302, P<0.05) were both positively correlated with the Lee's

pathological grade in children with IgAN, and the expression level of E-cadherin was negatively correlated with the Lee's pathological grade (r=-0.386, P<0.01).
Conclusions: Hyperuricemia is an important risk factor for poor renal outcome in children with IgAN. The PI3K-Akt-mTOR signaling pathway was overactivated in IgAN children with hyperuricemia, which may play an important role in the progression of renal fibrosis in children with IgAN promoted by hyperuricemia.
Keywords: Hyperuricemia; Immunoglobulin A nephropathy; renal fibrosis; PI3K-Akt-mTOR; children

Transition to adult care (and other psychosocial issues)

P2-395 - Preparedness to transition to adult care in pediatric kidney transplant recipients at a high volume, urban transplant center.

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Introduction: Inadequate transition readiness from pediatric to adult care is associated with poor outcomes, including loss of transplant and initiation of or return to dialysis. Graft failure rate is reported to range from 30% to 35% among renal transplant youth after transition to adult providers. It is important to assess and support transition preparedness as a part of health care management in pediatric patients from pre- or early teen years.
Methods: Participants were 72 post-kidney transplant patients aged 12 years and up followed at a major pediatric hospital. Mean age at participation was 18.6 years and mean age at transplant was 12.6 years. Patients were assigned to one of four phases of transition readiness based on clinical interviews on developmentally appropriate engagement in healthcare management. 26 patients were also administered the STARx Questionnaire and the Readiness for Transition to Adult Care Assessment Tool.
Results: At two years of start of the program, 8 patients (11%) were assigned to Phase 1, 15 patients (21%) to Phase 2, 15 patients (21%) to Phase 3, and 34 patients (47%) to Phase 4. 15/72 (44%) patients assigned to Phase were transitioned to adult providers. On the STARx Questionnaire, patients reported lowest average scores on asking providers about medical care (mean= 2.9 on a scale of 1-5) and using internet, books, or other guides to learn more about illness (mean= 2.6). The average score for preparedness for transition was 6.8 (0-10 scale) and for confidence in transition success was 6.4(0-10 scale).
Conclusions: Establishing and implementing a transition program is feasible as well as helpful to identify and support patients struggling with developmentally appropriate healthcare engagement. Patients may benefit from improving communication with providers and learning about illness from different resources.

Transition to adult care (and other psychosocial issues)

P2-396 - Moving the Needle: A Quality Improvement Intervention to Improve Transition of Care Discussion with Adolescent and Young Adult Patients with Kidney Disease

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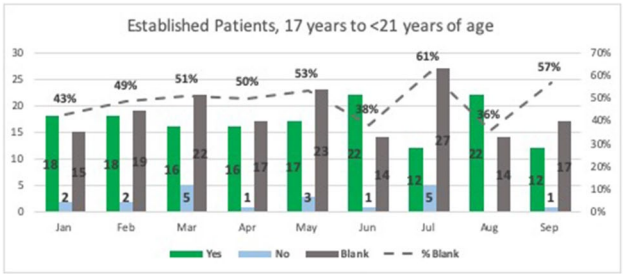
Background and objective: Studies reveal that adolescent and young adult (AYA) patients with chronic disease experience poor long-term outcomes during transition from pediatric to adult healthcare. Planned transition helps alleviate AYA patient and caregiver anxiety as well as improve retention in care and outcomes. We instituted a quality improvement (QI) project to plan transition of AYA patients. We aimed to increase documentation of standardized transition related discussion in electronic medical records (EMR) of 17-21-year-old AYA followed in our pediatric nephrology clinic from <5% to >50% over a 9-month period.
Methods: The effort was led by a nephrologist, along with EMR specialists. Several initiatives were implemented, starting with increasing provider awareness, development of a transition planning EMR smart-phrase, reminder signage posted in clinic, weekly review of provider EMR smart-phrase compliance, as well as stakeholder perspective from clinic personnel.
Results: Transition readiness discussion and documentation improved from <5% (December 2020) to overall 52% (January-September 2021).



Conclusion: Providers showed high interest in standardizing the pediatric to adult transition process, including documentation and planning of services for AYA transition. We noted that simply having a transition planning EMR smart-phrase increased discussion of transition, but external prompts were needed to remind providers to utilize the smart-phrase. We thus developed a "Transition" best practice alert in the EMR that is embedded within the provider workflow, and we will continue to monitor sustenance of the new process.

Transition to adult care (and other psychosocial issues)

P2-397 - What are the psychosocial factors influencing access to kidney transplantation and transplant outcomes for children? A Systematic Literature Review

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Introduction: Although kidney transplantation is often seen as the gold standard treatment for children and young people (CYP) with stage 5 Chronic Kidney Disease (CKD5), psychosocial factors have been cited as a barrier to accessing one. It is not clear what these factors are.
This study, through a systematic literature review, explores the breadth of psychological and social factors that delay or facilitate access to kidney transplantation for CYP with CKD5. This includes factors that influence kidney transplantation outcomes and factors deemed important to the quality of life of patient families.
Material and methods: We included peer-reviewed primary data from quantitative, qualitative and mixed-method studies. Medline, PsycInfo,

CINAHL and Web of Science were searched for papers published in English between January 1964 and September 2020.
Results: Once duplicates were removed, a total of 6235 studies were retrieved through database searches, handsearching references and consulting experts in the area. Fifty-seven studies remained after full-text screening against inclusion criteria. There were 46 quantitative, 8 qualitative and 3 mixed-method studies. Factors influencing access to transplantation included maternal education, social support network and therapy nonadherence. Race, socioeconomic status and geographic remoteness were often cited as contributory factors. Although factors such as anxiety, depression and avoidant coping strategies were described in the literature in relation to patient family experience and wellbeing, there was limited evidence linking these with accessibility to, or outcomes of, paediatric kidney transplantation.
Conclusions: Longitudinal and prospective studies are needed to fully assess the relationship between psychological factors and the relationship with social factors and a CYP's subsequent access to, or outcomes after, kidney transplantation.

Transition to adult care (and other psychosocial issues)

P2-398 - Emotional and behavioural function of children with chronic kidney disease

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Background: Chronic kidney disease (CKD) is associated with neurodevelopmental changes and poorer long-term neurocognitive outcomes in children. Despite the importance of psychosocial development in childhood, few studies have comprehensively assessed emotional-behavioural functioning in children with CKD.
Methods: We included 53 participants (aged 6-18 years) with CKD stages 1-5 (n=27), on dialysis (n=3) or with functioning kidney transplant (n=23) from three centres in Australia from 2015-2019. The Behaviour Assessment System for Children, 2nd edition (BASC-2) was used to assess children's psychosocial development in four areas: externalising problems (hyperactivity, aggression, and conduct problems), internalising problems (anxiety, depression, and somatisation), behavioural symptoms (atypicality, withdrawal, and attention problems) and adaptive skills (social skills, leadership, activities of daily living, functional adaptation, and adaptability).
Results: Participants' median scores on the BASC-2 Parent Report Scale (PRS) fell within the normal range for all domains assessed, except for somatisation which fell in the "at risk" range. However, an increased proportion of children with CKDwere in the "at risk" range for depression (22%), somatisation (24%), internalising symptoms (20%), withdrawal (20%), attention difficulties (18%), social skills (24%), leadership (24%) and activities of daily living (26%). Additionally, there was an increased proportion of children in the "clinically significant" range for all domains except leadership and adaptive skills.
Conclusions: Although children with CKD on average have behavioural scores within the normal range, there is a higher proportion of children who demonstrate, or are at risk for, psychosocial issues, particularly in the areas of adaptive skills and internalising problems.

Transition to adult care (and other psychosocial issues)

P2-399 - Estimated glomerular filtration rate in adolescents transitioning to adult care: two new equations and related calculators

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Estimation of glomerular filtration rate (GFR) during the transition to adult care must be conducted using the best available tools. The Schwartz bedside equation underestimates and the CKD-EPI overestimates GFR in adolescents and young adults. Several equations have been developed to solve this problem. The most recent are the CKiD under 25 (CKiDU25) and European Kidney Function Consortium (EKFC) equations. The purpose of our study was to compare these equations and related calculators for GFR estimation in adolescents.
Methods: We estimated GFR based on creatinine using the EKFC calculator (https://www.chuliege.be/jcms/c2_23005146/nl/nephrologie/ documents-pour-les-professionnels-de-la-sante) and CKiDU25 calculator (https://ckid-gfrcalculator.shinyapps.io/eGFR/) in 287 seventeen-year old patients (47.4% females) with CKD or/and AKD without AKI who were hospitalized at the Voronezh Regional Children's Clinical Hospital. The absolute difference was calculated by subtracting CKiDU25 values from EKFC values. The results were presented as a median and interquartile range [IQR].
Results: The median eGFR values for males using the Schwartz bedside, age-dependent CKiDU25, and EKFC were 82 [72–91], 100 [87–111], and 93 [82–106] mL/min/1.73m2, respectively, and those for females were 98 [85–110], 98 [85–109], and 104 [87–110] mL/min/1.73m2. The median absolute difference between EKFC and CKiDU25 in males was -6,7 [(-9.5)– (-3.7)], and that for females was 2.7 [(-0.3)–5.9] mL/min/1.73m2. Only 27 adolescents (9.4%) needed to reclassify their KDIGO GFR categories when switching from one equation to another. The CKiDU25 calculator estimates GFR, but also provides the interquartile range of the estimated GFR. The EKFC does not require height measurements, and EKFC values in 286 patients (99.7%) were less than the third (75th) quartile of the CKiDU25 estimation, which makes the EKFC useful screening tool.
Conclusions: GFR estimation using the interquartile range (provided by CKiDU25 calculator) opens new perspectives on eGFR and helps understand estimation limitations. EKFC is a useful tool for screening CKD in adolescents.

Transition to adult care (and other psychosocial issues)

P2-400 - Psycho-social impact of chronic renal failure on Tunisian children and adolescents: Study of 10 cases

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Introduction: Experiencing chronic somatic health issues can have serious consequences on children's mental and psychosocial health and impact their psychic development.
Objective: Assessing the impact of chronic renal failure on the children's mental health.
Methods: A descriptive cross-sectional study of children with chronic renal failure admitted to department of pediatric nephrology at Sahloul University Hospital (Sousse-Tunisia) from October to December 2021. We used the child depression inventory (CDI) and the strengths and difficulties questionnaire (SDQ) for parents to assess the social, behavioral, and emotional functioning of children.
Results: Our study involved 10 patients aged between 7 and 16, the average age was 12 years old, with a sex ratio of 0.6. 40% were middle school students; 40% were enrolled in primary school and 20% were students who dropped out after the diagnosis of their disease. The mean age at disease onset was 9 years and the mean duration of evolution was 5 years. 80% were on hemodialysis.**The CDI scores** ranged between 8 and 20 with two patients (20%) having scores above the threshold of 19. A psychiatric disorder according to DSM5 criteria was found in 70% of cases. **SDQ scores** ranged from 16 to 28, with abnormal scores in 80% of cases (>17) indicating severe socio-emotional difficulties. There was a significant association between age at the onset of disease and the SDQ score (p=0.035).
Conclusion: The impact of chronic kidney failure on children's mental health is significant. Early detection of psychological disorders is essential, to promote the well-being of these children and offer services that meet their needs.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-402 - A case of topiramate-associated hypokalemia in a with as yet undiagnosed Gitelman syndrome.

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We report a case of a 19-month old boy with epilepsy, infantile spasms, and global developmental delay who presented with isolated hypokalemia routine labs. His seizure disorders were managed with keppra, clobazam, and topiramate. His potassium had been largely normal over the course of his life (3.4-5.0 mM), though low once in the context of illness (2.4mM), until a dose increase in topiramate to help control seizures at 16 months of age. Though not present initially, repeated lab work demonstrated mild hypomagnesemia and metabolic acidosis. Urine studies demonstrated an inappropriately alkalotic pH with a positive urine anion gap, suggestive of a mild renal tubular acidosis. Topiramate associated with proximal and distal tubular dysfunction, and the pathophysiology of this will be reviewed here. Our patient was treated with potassium citrate supplementation, which provided rapid correction of hypokalemia, as well as magnesium supplementation, correcting the hypomagnesemia. Furthermore, his topiramate was gradually weaned off.
During his hospitalization, he was also noted to have poor weight gain over several months, as well as several subtle dysmorphisms. He was the product of a consanguineous union and prior gene panel for infantile epilepsy did not identify a cause for his seizures. As such, trio-whole exome sequencing was performed and demonstrated a homozygous frameshift mutation in the SLC12A3 gene, with each parent carrying one copy of the mutation. He was therefore diagnosed with Gitelman syndrome. No mutations were identified that explained his seizure disorder. While it is rare for Gitelman syndrome to present under the age of 6, it is possible that our patient's presentation was exacerbated by topiramate. In fact, KDIGO consensus guidelines expressly discourage topiramate use in the setting of Gitelman syndrome, though to the best of our knowledge, the potential adverse outcomes of this have not been demonstrated in the literature until now.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-403 - cystinosis revealed by metabolic alcalosis : case report

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Background: Cystinosis is a rare autosomal recessive lysosomal disease,signs are secondary to accumulation of cystine crystals in various organs including kidneys, eyes, liver and brain. Infantil cystinosis is being the most frequent form, it is associated with failure to thrive, recurent episodes of dehydration and fonconi syndrome with hypophosphatemia, severe metabolic acidosis, rickets and visual impairment, it can lead to renal failure and blindness
Method: We report a case of 3 year old boy, followed up since age of one year for Bartter syndrome
Results: 3year and 6 month old boy, reffered for follow up of bartter syndrome case diagnosed at the age of one year**,** history of parental consanguinity, full term of terun event full pregnancy and normal delivary, birth weight 3.5 kg and normal APGAR score, Frequent admissions since the age of 3 month for dehydration**.** At the age of one year he was admitted in pediatric hospital for severe malnutrition, polyuria, polydipsia, hyponatremia sodium 125 meq/l, hypokaliemia 2 meq/l, hypochloremia 80 meq/l, normal calcium and phosphorus, metabolic alcalosis ph 7.5 hco3 28 meq/l, high renine 75 mg/ml and high aldosterone 780mg/dl. Urine analysis was negative to blood, protein,and glucose, no rickets signs and renal fonction was normal, so diagnosed and treated as case of Bartter syndrome
At the age of 3 year, the child was reffered to our hospital for rickets. He has severe malnutrition and corneal cystine crystals detected on ophtalmologic examination
Conclusion: Cystinosisis a rare disease, diagnosed ussually as Fonconi syndrome with matabolic acidosis, rare cases are Bartter syndrom like with hypochlormic metabolic alcalosis wich can lead to late diagnosis

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-404 - Secondary pseudohypoaldosteronism associated with urinary tract infection and cytomegalovirus infection in two infants

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Aim: Secondary pseudohypoaldosteronism (sPHA)also named transient pseudohypoaldosteronism is a life-threatening condition in infancy. To improve awareness of this condition, we present 2 cases to highlight the clinical features of sPHA.
Methods: The authors retrospectively reviewed the clinical data, treatment and prognosis of 2 infants with sPHA associated with urinary tract infection, urinary tract malformations and cytomegalovirus infection admitted to our hospital.
Results: Both cases were male and diagnosed at 4 months of life with sPHA. Both cases developed transient aldosterone resistance. Cardiac arrest occurred in 1 case.
Conclusion: After appropriate treatment, sPHA achieved a complete remission in both cases. Cytomegalovirus may be involved in the pathogenesis of sPHA.
Keywords: pseudohypoaldosteronism;mineralocorticoid resistance;tubulopathy;urinary tract malformation;cytomegalovirus

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-406 - Presence of renal giant mitochondria as an early diagnostic sign in a case of Fanconi syndrome with asymptomatic MODY1

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Introduction: Maturity-onset diabetes of the young 1 (MODY1) is characterized by macrosomia and transient hypoglycemia in neonates, in addition to diabetes mellitus (DM). Only patients with MODY1 harboring p.R63W are sure to develop Fanconi syndrome (MODY1/FRTS), and patients with the other MODY1 mutations are not. Here we report the successful diagnosis of MODY1 in a patient harboring p.R63W before confirmation of DM-related hyperglycemia by blood test, alerted to the presence of abnormal mitochondria in a kidney biopsy specimen revealed by electron microscopy.
Case report: The patient was born at 39 weeks of gestation with macrosomia, elevated levels of liver enzymes, and transient hypoglycemia. At three years of age, he underwent a urine dipstick test, which revealed proteinuria. He was referred to our hospital, and further laboratory investigations revealed metabolic acidosis, renal dysfunction (estimated GFR 57 mL/min/1.73 m²), hypouricemia, proteinuria, aminoaciduria, and glycosuria. On this basis, we diagnosed him as having Fanconi syndrome and performed percutaneous renal biopsy. Light microscopy revealed no evidence of proximal tubule disorder, but electron microscopy demonstrated mitochondria with disordered cristae in glomerular podocytes and giant mitochondria in proximal tubules. Mitochondrial nephropathy was suspected, and the patient's skin fibroblasts grown on galactose medium showed a decreased oxygen consumption rate suggestive of mitochondrial dysfunction. Therefore, genetic testing was performed and a *HNF4A* gene mutation (c.187C>T; p.R63W) was detected. At the time of MODY1/FRTS confirmation, the patient had not developed DM.
Discussion: A few previous reports have suggested that MODY1 is associated with mitochondrial dysfunction, increased lipid droplets, and abnormal mitochondria based on electron microscopy studies of HNF4A-depleted Drosophila nephrocytes. Because treatment of MODY1 differs from that of typical type 1 or type 2 DM, and diagnosis of MODY1 is often difficult, early diagnosis using renal electron microscopy is very important for MODY1/FRTS patients.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-407 - Forty years experience in Bartter's syndrome

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Bartter syndrome (BS) is a rare disease involving the ascending limb of the loop of Henle, affecting 1/ 1000000 individuals, with autosomal recessive inheritance.
A descriptive, observational and retrospective study was performed. The aim was to describe the long-term evolution of children with SB, referred to our clinic since 1969.
We described 19 cases (9 females/10 males) with clinical criteria of BS, 10/19 with genetic confirmation (Table 1). 11/19 had nephrocalcinosis at diagnosis, 5/5 with KCNJ1 mutation and 1/5 with CLCNKB mutation. 12/16 presented with polyhydramnios during pregnancy, 3 were not recorded in the history. 12/17 consulted by digestive symptoms and growth failure. 5/17 had electrolyte disturbances in the neonatal period. Mean height at the first visit was -2.1±1.65 SD, median -1.58 (-4.62-0.82 SD). Median age at last visit was 17.08 (5.05-27.3 years). 19/19 received prostaglandin inhibitors (NSAIDs) indomethacin (maximum 2.04±0.68 mg/kg/day) or tolmetin (maximum 31.2±14mg/kg/day), with no significant adverse effects, permitting treatment to be maintained throughout the course of the disease. 19/19 required a mean potassium intake of 4.4 (0.5-15 meq/kg/day) and 6 required magnesium supplementation. 12/15 required hospital admission, 10 coinciding with gastrointestinal symptoms and 2 with symptoms of hypokalemia due to poor adherence to treatment. The median number of admissions was 1 (0-14). Mean height at the last visit was -0.98 ±1.08 SD, median -1.16 (-2.99 and 0.88). At the end of evolution 3 had chronic kidney disease stage II, all with nephrocalcinosis. The median Schwartz estimated glomerular filtration rate is 101 ml/min/1.73m2 (71-164).
The evolution of patients with BS has been satisfactory, with good ambulatory control. At the end of the follow-up only 1 has a lower height -2SD. Renal function is deteriorated in only those with nephrocalcinosis, although we are uncertain about the role of NSAID use in the long-term.

	KCNJ1 (n=5)	CLCNKB (n=5)
Polyhidramnios	4/5	4/4
Age diagnosis (months)	1,6±2,6	10±14
Clinical features at diagnosis	hyperkalemia metabolic alkalosis	Gastrointestinal symptoms and growth failure
Nephrocalcinosis	5/5	1/5
K intake (meq/kg)	3,5±3,4	8,8±3,8
Height at diagnosis (SD)	-3,49±1,23	-1,53±1,1
Final Height (SD)	-1,4±0,94	-0,84±1,5
Final glomerular filtration (ml/min/1,73m2)	86±8,8	127±27

Table 1. Clinical features in BS with genetic confirmation.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-409 - Two cases of tubulointerstitial nephritis with uveitis syndrome that presented with anorexia as the first symptom

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Background: Tubulointerstitial nephritis with uveitis (TINU) syndrome is a rare disease in children, with clinical manifestations that differ from case to case. Here, we describe two cases of TINU which presented with anorexia as the first symptom.
Case 1: A 14-year-old girl presented with anorexia. She also had painful bloodshot eyes and photophobia 10 weeks after the third shot of HPV vaccination. A local ophthalmologist diagnosed her as bilateral uveitis and refer her to our hospital. Laboratory findings revealed elevated serum creatinine and highly increased urinary beta-2 microglobulin. Considering also the result of 67Ga-citrate scintigraphy which demonstrated significant renal uptake, the diagnosis of TINU syndrome was made. Oral and topical corticosteroid therapy relieved her symptoms.
Case 2: A 14-year-old girl presented with fatigue, anorexia and weight loss. She visited a local doctor, who noted high serum creatinine level. Tubulointerstitial nephritis was suspected, and she was referred to our hospital. Tubulointerstitial nephritis was diagnosed by renal biopsy and a course of oral corticosteroid was started. Four months after the start of treatment, cyclosporine was added because serum creatinine rose again with gradual corticosteroid reduction. One more month later, she developed bilateral uveitis and was diagnosed with TINU syndrome. Now 3 years later, her renal function remains improved after cessation of oral corticosteroid and cyclosporine, but she continues to receive topical corticosteroid therapy for uveitis.
Conclusion: Both of two cases firstly presented anorexia. It is relatively common that teenage patients visit us for nonspecific symptoms like fatigue and anorexia, especially in this SARS-CoV2 pandemic period. An increasing number of patients present with anorexia as their chief complaint, and they should not be assumed as psychsomatic disorders, since their complaints could be part of the symptoms of tubulointerstitial nephritis.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-410 - Cellular senescence is associated with CKD progression in childhood cancer patients with karyomegalic interstitial nephropathy

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Background: Karyomegalic interstitial nephropathy (KIN) is described as a tubular nephropathy with abnormally enlarged, irregular and hyperchromatic nuclei of tubular epithelial cells (TECs). The histologic pattern was first described in patients with FAN1 mutations with defective DNA damage repair. The same histological features are infrequently reported in children treated for childhood cancers with the alkylating agent ifosfamide.
Methods and results: We here report that KIN could be diagnosed in 6 consecutive children treated for childhood cancer biopsied for chronic kidney disease (CKD) with low molecular weight LMW proteinuria of unknown cause between 2018 and 2021.
Features of karyomegaly and senescence were identified in TECs of these patients by automated morphometric assessment of nuclear size distribution, and immunohistochemical markers for DNA damage (γH2AX), cell-cycle arrest (p21+, Ki67-), and nuclear lamina decay (loss of lamin B1). The number of p21 positive cells by far exceeded the typically very small numbers of truly karyomegalic cells. P21 positive TECs were found to contain significantly less lysozyme, testifying to defective resorption as an explanation of the consistent finding of LMW proteinuria. Moreover, in the 5 patients with the largest nuclei, the percentage of p21-positive TECs showed strong inverse correlation with change in eGFR from biopsy to last follow-up (R^2=0.93, p<0.01).
Conclusion: Karyomegaly and cellular senescence-associated tubular dysfunction appear to be a more prevalent, rather than rare, cause of otherwise unexplained CKD and LMW proteinuria in children treated for cancer with ifosfamide. This finding may have important implications for future personalized treatment strategies.

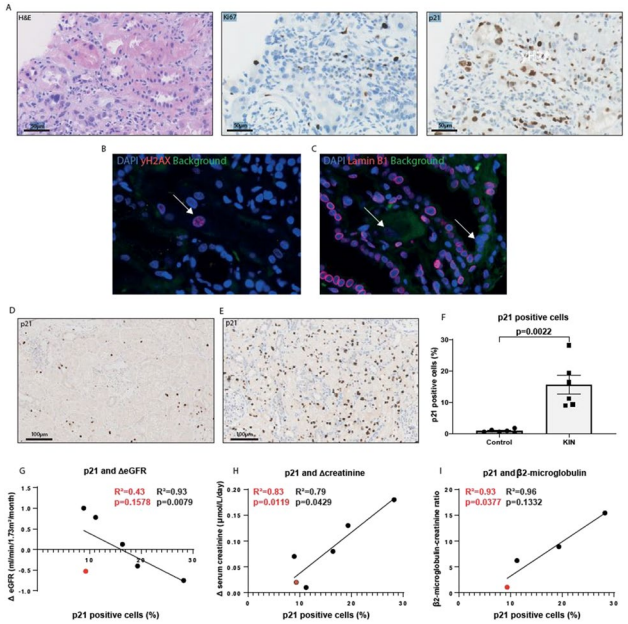

Figure 1A. Enlarged nuclei are Ki67 negative, p21 positive in KIN, **(B-C)** yH2AX positive, and show less LaminB1 staining in KIN. **(D-F)** p21 staining in controls and KIN **(G-I)** Correlations between p21positive cells and renal function markers. Values in red include the biopsy with the smallest nuclei and values in black exclude the smallest nuclei.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-411 - Benign isolated chronic proteinuria in a young child with FMF?

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Introduction: Familial Mediterranean Fever (FMF) is an auto-inflammatory disease characterized by recurrent fever and associated with the development of chronic renal disease with proteinuria during long-term follow-up. We describe the evaluation of proteinuria in a young child with FMF.
Case report: A young boy of with recurrent fever was diagnosed with FMF at the age of 3 years (heterozygous *MEFV*mutation). During follow-up he demonstrated persistent, isolated, non-nephrotic proteinuria (18-20 mg/m2/hr. (N<4)). Serum creatinine was normal. Additional analysis: tubular proteinuria: alpha 1-microglobuline (32.7 mg/g creatinine (<11 mg/g), no other signs of renal tubular disease. Serum amyloid A was

slightly elevated 8mg/L (<4mg/dl). A renal biopsy was normal and proteinuria did not respond to RAAS blockade. Family screening demonstrated similar findings in sister (isolated proteinuria: 19mg/m2/hr.) A genetic panel demonstrated heterozygous class 3 and 4 *CUBN* mutations in both sibs, associated with Imerslund-Gräsbeck syndrome (IGS). However, next to proteinuria, IGS is characterized by vitamin B12 deficiency and megaloblastic anemia, which both kids did not have?
Discussion: Cubilin is a tubular uptake receptor containing 27 CUB domains for ligand binding and is expressed in the small intestine and proximal tubule. In 2020 Bedin et al. discovered C-terminal CUBN variants associated with chronic proteinuria and normal kidney function, but without hematological abnormalities associated with IGS. The location of these mutations leads to modifications after the vitamin B-12 binding domain (CUB5-8) and is considered a novel diagnosis: isolated chronic benign proteinuria (OMIM #618884). The mutations of our siblings are located at domain 20 and 21, confirming this diagnosis.
Conclusion: We stress the importance evaluating an odd presentation of proteinuria in a patient with a high risk for kidney disease and "Isolated chronic benign proteinuria" should be taken into consideration in the differential diagnosis of unexplained (tubular) proteinuria.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-412 - Fanconi syndrome related to deferasirox in transfusion-dependent patients

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Introduction: Iron chelators are necessary in transfusion-dependent patients to prevent secondary haemochromatosis. Deferasirox has been used as an effective and convenient once-daily oral chelating agent, however its possible renal tubular toxicities should be monitored.
Case Presentations: Case 1: A 5-year-old girl with transfusion-dependent sideroblastic anaemia received oral deferasirox for 2.5 years. Her routine blood monitoring showed normal anion gap metabolic acidosis with serum bicarbonate 12.7 mmol/L. She had hypokalaemia at 3.0 mmol/L, with elevated trans-tubular potassium gradient (TTKG) of 5.6. Her serum phosphate level was borderline low at 1.06 mmol/L, with tubular reabsorption of phosphate (TRP) of 73.2%. Besides, her urine sample showed generalised aminoaciduria, with overall clinical presentation consistent with Fanconi syndrome. Her deferasirox was withheld, and her metabolic acidosis and electrolyte disturbance improved with intravenous sodium bicarbonate followed by oral potassium citrate. Her deferasirox was resumed 2 weeks later at a lower dose, and her potassium citrate was taken off 6 months later.
Case 2: A 19-year-old girl with transfusion-dependent thalassaemia on oral deferiprone as iron chelator added oral deferasirox 4 years ago due to suboptimal iron chelation. Blood monitoring showed hypokalaemia 2.8 mmol/L and hypophosphataemia 0.68 mmol/L, with TTKG and TRP 6.4 and 76.6%, respectively. Her blood gas showed normal anion gap metabolic acidosis with serum bicarbonate 19 mmol/L. There was also generalised amino acid loss in her urine. She was treated with oral potassium citrate and phosphate-sandoz effervescent tablets. Her oral deferasirox was discontinued, and subcutaneous deferoxamine was started later for iron overload. Her electrolyte supplements were stopped after 4 months.
Conclusion: Oral deferasirox can lead to Fanconi syndrome, which may develop several years after initiation of the medication. As the patients can be asymptomatic, interval blood tests are recommended for early detection and treatment to prevent potentially life-threatening electrolytes and acid-base disturbances.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-413 - The case of early blood vessels intervention in infant idiopathic fanconi syndrome.

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Objectives: Fanconi syndrome, a proximal tubular disease,is known to have a large genetic predisposition when diagnosed in childhood, and the prognosis is often poor due to these genetic causes.
Methods: We report a case of a young 6 months old baby diagnosed with an idiopathic fanconi syndrome in which an early chemport insertion was helpful.
Results: A 6-month-old baby presented with intermittent fever and growth retardation. The patient's urinalysis, showed not only renal glycousria, but also proteinuria and increased phosphorus secretion and he were diagnosed as Fanconi syndrome. We performed genetic studies but only a variant of uncertain significance(VUS) was identified. As a result, the causative gene for Fanconi's syndrome was not identified, and the patient was treated for idiopathic Fanconi's syndrome that occurred in infancy.The patient was repeatedly hospitalized for dehydration, infection, hypoglycemia associated with idiopathic Fanconi syndrome up to 18months of age. Many times, an experienced intravenous nurse often had to try more than three times to secure the patient's IV line. The patient also had to be considered for enteral nutrition through a tube instead of supplying fluid through blood vessels, but with enteritis, it was challenging. . However, having chemport insertion done, fluid administration became possible and the number of hospitalizations greatly decreased. Nowadays, the patient is receiving tube feeding and oral rehabilitation? as he showed oral feeding difficulties.
Conclusions: Fanconi syndrome diagnosed infancy often present with poor prognosis, coupled with a genetic predisposition. In this case of frequent hospitalization due to problems such as repeated dehydration and infection during the clinical course of these patients, an early intervention to secure blood vessels via central line is thought to improve the course of the disease and reduce the number and the interval of hospitalization.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-416 - Kidney function evaluation of Mexican pediatric patients with glycogen storage disease I

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Introduction: GSD Ia is caused by variants in the G6PC gene, while type Ib is caused by variants in SLC37A4. Both entities may share clinical features, including alterations in renal function, such as distal renal acidification defects, hypercalciuria, decreased citrate excretion, hyperfiltration and microalbuminuria. The aim of this study was to identify renal alterations in Mexican patients with GSD with a specific renal evaluation.
Methods: Cross-sectional study, patients with molecular diagnosis of GSD Ia and GSD Ib were assessed. The specific renal evaluation consisted of blood gas, serum anion gap (BAS), creatinine, uric acid, general urine test (GUT) to evaluate proteinuria, glycosuria and microalbuminuria. In case of urinary pH > 6.5, acidification test was performed with furosemide at 1 mg/kg. Alkalinizing treatment was suspended 7 days prior to renal evaluation.
Results: 10 patients were included (6 GSDIa, 4 GSDIb), with a median age of 10.5 years, 8 of 10 patients were women, all patients had a diagnosis of distal RTA and 9 had alkalinizing treatment prior to evaluation. The use of bicarbonate and citrates with potassium were the most used treatments. After the evaluation of the patients with GSD Ia, 3 had no kidney involvement, 2 had hyperfiltration, and 1 patient had hyperfiltration plus microalbuminuria. Patients with GSD Ib only 1 presented hyperfiltration, 3 of them had no renal involvement. (Table 1).

Tabla 1. Description of general characteristics of the pediatric population with GSD Ia and GSDIb

	GSD Ia n= 6	GSD Ib n=4
Age (year), median min - máx	10.5 (0.5 – 14)	6 (5-14)
Sex, women, n	5	3
Height (z score), median min - máx	- 0.84 (-4.1 – 0.5)	- 2.96 (-3.0 – -2.6)
Short strature, n	3	4
Alkalizing treatment prior to assessment, n	6	3
Type of alkalizing treatment		
Citrates with K	1	3
Citrates without K	2	-
Bicarbonate	3	-
Renal diagnosis at the end of the evaluation		
No renal disfunction	3	3
Hyperfiltration	2	1
Distal RTA	-	-
Proximal RTA	-	-
Others	1	-

Conclusions: This work is a pioneer in our country. The most frequent renal finding was hyperfiltration that required the use of enzyme convertase inhibitors, which had not been detected or was associated with the erroneous diagnosis of distal RTA, which means treatment delay. A targeted and specific assessment in patients with glycogenosis I is essential to objectively identify the renal alteration they present.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-417 - Outcomes of 23 patients with cystinosis from a single center

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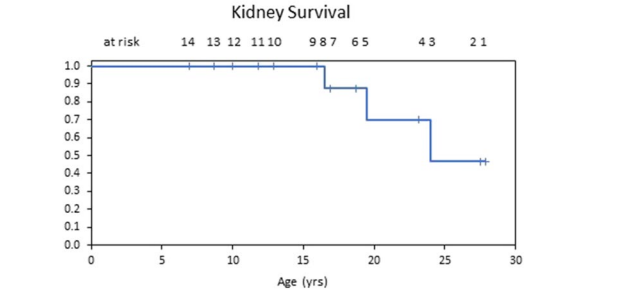
Methods: Patients seen at a single centre were reviewed. Data are given as median (range).
Results: Of 23 patients, 9 transferred into the program, 5 as adults. Three adolescent presentations were diagnosed at 10 (9-11) years, those with infantile cystinosis at 1 (0.1-2.7) years old. Follow-up was for 8.6 (1.3-27.6) years. Four are sib-pairs with the diagnosis of the younger made either soon after an initial adolescent presentation or by a WBC cystine level just after birth. Three patients are no longer followed (one died and two moved). The remaining 20 are 22.3 (5.7-55.4) years old.
Four patients required treatment for hypothyroidism, two of whom presented with adolescent cystinosis. Only two had diabetes both with adolescent cystinosis. For all patients seen 10 (43%) reached kidney failure at 16.3 (12.2-25.7) years of age and received a kidney transplant with one transplant still functioning after 40 years.
When last seen the 14 patients followed from diagnosis were 17.1 (6.9-31.2) years old. Mixed leukocyte WBC cystine levels (nmol 1/2cystine/mg protein) were:

At diagnosis 1.41 (0.85–3.82)
Average on treatment

	Overall	up to 10 yrs of age	10 to 20 years of age	over 20 years of age
Median	0.25	0.26	0.24	0.12
Range	0.15 - 0.42	0.14 – 0.51	0.11 – 0.33	0.11 – 0.42
avg #/patient	68	34	30	26
#patients	14	14	11	5



None of these 14 patients have hypothyroidism or diabetes. Their height SDS is -1.1 (-3.62-0.39). Three had kidney failure at age 19.5 (16.5-24) years. Survival analysis shows a median age of 24 years for kidney failure. One patient with maintained native kidney function has delivered two healthy babies. One patient has received a stem cell transplant and is not taking cysteamine.
Conclusions: For patients seen from diagnosis, with the use of growth hormone in a majority, the median HSDS was higher at -1.1 than in in a large European cohort. The average WBC cystine levels between 10-20 years were not higher than <10 years of age and kidney survival longer at 24 years than 19.5 years in a large European 1990s cohort. For infantile cystinosis, with low WBC cystine levels, non-renal sequelae appear unlikely before 30 years.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-418 - SLC12A1 mutation associated with Type 1 Bartter's Syndrome and Hyperparathyroidism.

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Background: Bartter's Syndrome (BS) is characterised by hypokalemia, metabolic alkalosis, hypercalciuria and nephrocalcinosis.
Type 1 BS is modulated by the Solute Carrier Family 12 (SLC12A1) gene, which in turn encodes the furosemide sensitive, sodium (N) - potassium (K) - chloride (C) co-transporter (NKCC2). A very small number of cases have been published that describe Type 1 Bartter's syndrome in conjunction with hyperparathyroidism and associated SLC12A1 mutation.
Case Report: The subject was born to consanguineous parents of Arab origin. On day 2 of life, the subject was admitted to a paediatric intensive care unit (PICU). Her main issues were dilated cardiomyopathy, hypocalcemia and hypokalemia. Hyponatremia,

hypochloremia and metabolic alkalosis developed over the course of her admission with resolution of her cardiomyopathy.
Initial PTH in PICU was 50.9 (11-35). Maternal calcium and vitamin D were normal. A clinical diagnosis of Bartter's syndrome was made in light of hyponatremia, hypokalemia and metabolic alkalosis followed by genetic confirmation of homozygous SLC12A1 mutations on whole exome sequencing. PTH remained elevated over a 4 year follow up.
Discussion: As demonstrated by the case we have described above and the extremely small number of similar cases that are described in available medical literature, the association between antenatal Bartter's syndrome and hyperparathyroidism is a unique clinical phenotype. The exact role pathogenic SLC12A1 mutations play in leading to such marked hyperparathyroidism is unclear. Whether the hyperparathyroidism associated with SLC12A1 is a separate clinical entity or as a result of the Bartter's syndrome phenotype is not clear.
To date, these patients have been managed with a combination of NSAID's and calcimimetic drugs. However, there is relatively sparse data or reports regarding long term bone health in these patients or the potential for novel therapies.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-420 - A case of secondary pseudohypoaldosteronism associated with mild hydrouteronephrosis and afebrile urinary tract infection

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Introduction: Secondary pseudohypoaldsteronism (S-PHA) occurs in infants with urinary tract anomalies (UTA) and/or urinary tract infections (UTI). The symptoms of S-PHA are failure to thrive, vomiting, irritability and fever. The blood test shows hyponatremia, hyperkalemia and metabolic acidosis, which may be a life-threatening condition. Usually, UTA include bilateral high grade hydronephrosis or vesicoureteral reflux (VUR). Here, we report a case of a six-month-old boy, who did not show symptoms excepting weight loss, with unilateral hydroureteronephrosis and afebrile UTI.
Case: A six-month-old boy with an unremarkable past history including newborn screening showed weight loss (-260 g/two months). He had not any other symptoms such as vomiting or fever. Blood tests showed electrolyte abnormalities and metabolic acidosis without renal dysfunction (creatinine 0.26 mg/dL, sodium 121 mEq/L, potassium 5.5 mEq/L, pH 7.329, HCO_3^- 21.3 mEq/L). And aldosterone resistance was revealed (plasma renin activity 51 ng/ml/hour, aldosterone 20300 pg/ml). Urinalysis showed pyuria. After hospitalization, the electrolyte was normalized in three days with infusion therapy. Afterwards, he was diagnosed with UTI because of fever, then treated with antibiotics. *Escherichia coli* was found in culture. Ultrasonography revealed left hydroureteronephrosis (SFU grade1, ureter 7.5 mm) and VUR was not detected in voiding cystourethrogram. After discharge, adequate weight gain was observed. Three months later aldosterone resistance was normalized (renin activity 4.3 ng/ml/hour, aldosterone 63.1 pg/ml) and electrolyte supplementation was tapered off.
Conclusion: S-PHA is considered to be caused by combination of UTI with obvious UTA diagnosed in perinatal period, such as bilateral high grade hydronephrosis, VUR and solitary kidney. However, as this case, S-PHA could develop even with mild UTA and afebrile UTI. Because the symptoms of S-PHA are sometimes unnoticeable, patients with mild UTA should be observed carefully.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-423 - Etiology and outcomes in primary renal tubular acidosis

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Etiology and outcomes in primary renal tubular acidosis
Sukanya Priyadarshini, Aditi Sinha, Radhika Tandon, Kapil Sikka, Manisha Jana, Vijay Mathur, Pankaj Hari, Arvind Bagga
Introduction: Few studies have evaluated medium- to long-term outcomes and genotype phenotype correlation in renal tubular acidosis (RTA), particularly outside Caucasian cohorts.
Methods: Patients fulfilling clinical, radiological, and biochemical criteria of primary RTA were enrolled prospectively at a single tertiary care centre during 2020-2021. Evaluations included estimated glomerular filtration rate (eGFR), anthropometry, extrarenal manifestations, and where feasible, etiology based on clinical-exome sequencing.
Results: Of 58 patients (72.4% boys) enrolled, 33 had Fanconi syndrome, 24 had distal RTA, and one was diagnosed with type III RTA (**Table 1**). The most common inherited defects were in *CTNS* (proximal RTA) and *ATP6V1B1* (distal RTA). At median (interquartile range) follow up of 58 (42, 96) months, 52.7% were underweight and 76.4% had short stature. Extrarenal manifestations included cystine crystals (9/11 patients with cystinosis), sensorineural hearing loss (5/24 of distal RTA, including four with *ATP6V1B1* and one with *ATP6V0A4* variants), amelogenesis imperfecta (4 patients of distal RTA due to *WDR72* variant), hypothyroidism (9 patients, including 5 with cystinosis), fasting hypoglycemia (two patients with Fanconi Bickel syndrome), and deranged liver function (3 patients with tyrosinemia and two with Fanconi Bickel syndrome). The eGFR at last follow-up was 106.2 (81.2, 123.2) mL/min/1.73 m^2, with chronic kidney disease stage (CKD) 3-5 in 9 (16.4%) cases, chiefly in patients with nephropathic cystinosis (n=6).
Conclusions: Almost one-sixth of patients with primary RTA have progressive CKD by the age of five years, most commonly with nephropathic cystinosis. The majority of patients are undernourished, more often with Fanconi syndrome than distal RTA.

	Renal tubular acidosis	Fanconi syndrome	Distal renal tubular acidosis
Number (n,%)	58, 100%	33, 56.90%	24, 41.38%
Boys (n,%)	42, 72.40%	24, 72%	17, 70.83%
Age at enrolment (months)$	93 (58, 182.50)	71 (57, 154)	104.5 (59, 210)
Age at onset (months)$	12 (5, 26)	12 (5, 26)	18 (5, 34)
Duration since symptom onset (months)$	58 (42, 96)	56 (38, 81)	83.50 (45.50, 156)
Weight for age SDS$	-2.10 (-3.59, -0.78)	-2.70 (-4.62, -1.17)	-1.67 (-3.10, -0.75)
Height for age SDS$	-3.41 (-5.02, -2.12)	-4.56 (-5.82, -3.18)	-2.40 (-3.50, -1.76)
Underweight, n (%)	29 (52.73%)	20 (64.52%)	9 (39.13%)
Stunted, n (%)	42 (76.36%)	26 (83.87%)	16 (69.50%)
Serum HCO_3^- (mEq/L)	18.95 (15.35, 23.25)	19.20 (15.20, 23.70)	18.85 (15.60, 23)
Serum K^+ (mEq/L)	3.70 (3.24, 4.10)	3.70 (3.16, 4.20)	3.73 (3.35, 4.03)
Prevalence of medullary nephrocalcinosis	48.07%	33.33%	71.42%
eGFR (mL/min/1.73 m^2)$	106.20 (81.22, 123.20)	105.10 (60.70,119)	113.58 (86.14, 130.10)
Genotype		*CTNS* (11), *OCRL* (5), *CLCN5* (5), *SLC2A2* (6), *GATM* (1), *FAH* (3), idiopathic (1)	*ATP6V1B1* (8), *ATP6V0A4* (5), *SLC4A1* (4), *WDR72* (4)

Table 1: Baseline characteristics. $ - Median (IQR). One patient of type III RTA not included in the table. SDS – Standard deviation score, IQR – Interquartile range.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-424 - Proximal tubular injury induced by dietary phosphate load is linked to Stat3/Kim-1 signaling and macrophage recruitment in mice

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Objectives: High phosphate levels are linked to enhanced all-cause mortality and responsible for the progression of kidney damage in patients with chronic kidney disease. However, renal effects of chronic high phosphate load for healthy individuals are still vague.
Methods: C57BL/6N mice were fed a 2% high phosphate diet (HPD) for one to six months and compared to mice on 0.8% normal phosphate diet (NPD). Parameters of phosphate homeostasis and development of kidney injury were investigated. *In vitro* experiments using HK-2 proximal tubular (PT) cells were performed to study the impact of phosphate, fibroblast growth factor (FGF) 23 and parathyroid hormone (PTH) on tubular cell damage.
Results: HPD in mice caused hyperphosphatemia despite phosphaturia, increased FGF23 and PTH. Histopathological analysis revealed progressive PT injury in HPD-fed mice from two months onwards followed by a rapid progression from month 5 to 6 compared to NPD. This was accompanied by increased tubulointerstitial fibrosis. In PT of HPD-fed mice, increased Kim-1 expression was positively associated with tubular injury score and fibrosis. Histological staining revealed increased number of $pStat3^+$ cells that was associated with upregulated Kim-1 synthesis. The chemokine MCP-1 was upregulated in PT of HPD-fed mice and associated with Kim-1 expression indicating an interaction between pStat3/Kim-1 signaling and MCP-1. We demonstrated significantly increased recruitment of $F4/80^+$ macrophages around PT lesions of HPD-fed mice after three and six months that was associated with increased MCP-1 synthesis and tubular injury score. *In vitro* stimulation of HK-2 cells with FGF23 or phosphate, but not PTH, induced the phosphorylation of Stat3. Interestingly, only phosphate treatment significantly upregulated Kim-1 and MCP-1 expression.
Conclusions: High dietary phosphate load induces progressive PT damage stirred by Stat3/Kim-1 signaling mediating MCP-1-dependent macrophage invasion. Our data indicate a potential health problem due to high phosphate intake that demands for clinical studies on this issue.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-425 - A rare case of Acute Pancreatitis in a child with Infantile (Type 4) Bartter's syndrome

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Pancreatitis is a rare presentation in the paediatric population. It has previously been described in patients with Type 1 and 2 Bartter's syndrome. The object of this clinical case report is to highlight a case of pancreatitis in an infant with Type 4 Bartter's, an association not previously described in the literature.
A three year old boy with known Infantile Bartter's syndrome presented acutely unwell with Sars-CoV2 infection. He was born prematurely at 27 weeks, with his clinical progress to date complicated by necrotising enterocolitis, retinopathy of prematurity, recurrent central line infections and chronic kidney disease (eGFR 40). He was initially transferred from his local hospital to paediatric intensive for invasive respiratory support. Following improvement, he was discharged to ward-level care for ongoing recovery.
Seven days after discharge from intensive care, the patient began showing signs of discomfort, with teeth grinding, tachycardia and reduced feed tolerance. Inflammatory markers including CRP were markedly elevated. Renal function was significantly deranged (eGFR 15). An ultrasound scan identified a large pancreatic pseudocyst. Amylase was significantly elevated. The patient was treated with IV antibiotics, IV fluids and enteral feeding stopped. Fluid and electrolyte management became increasingly challenging, with the patient becoming increasingly distressed and fluid overloaded. Care was re-orientated after several days of treatment. This case adds to those previously reported in Type 1 and 2 Bartter's, and raises the likelihood that dysfunction of ROMK due to mutations is causative of pancreatic issues in these patients. This highlights the importance of considering pancreatitis in patients with this condition who present with signs of systemic illness.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-426 - Kawasaki disease and upper urinary tract infections have comparable tubular dysfunction

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Background: In renal disease, urinary β2-microglobulin (u-B2MG) is used as a marker of tubular dysfunction, especially renal tissue damages in upper urinary tract infection (U-UTI). Serum B2MG (s-B2MG) was known as a cytokine-induced protein to evaluate systemic inflammation in Kawasaki disease (KD). On the other hand, KD was also known to lead to renal tubular disorders such as tubulointerstitial nephritis. Therefore, it is difficult to determine which elevated u-B2MG in KD is systemic vasculitis or tubular damages. In this study, we compared the excretion rate of u-B2MG: fractional excretion β2-microglobulin (FEB2MG) in cases of KD and U-UTI, and investigated tubular damage in KD.
Methods: Subjects were 44 KD and 39 U-UTI cases admitted to our department from January 2018 to December 2021. Blood and urine samples were collected on the same day during fever and FEB2MG [(u-B2MG/s-B2MG)/(urinary Creatinine/serum Creatinine) x 100 (%)] was calculated. We performed voiding cystography to 39 cases with hydronephrosis on renal ultrasound examination, and divided into 15 cases with vesicoureteral reflux (VUR+) and 24 cases without VUR (VUR-).
Results: The results for KD and U-UTI patients were as follows: s-B2MG 2.1 ± 0.1; 2.3 ± 0.1 mg/L, u-B2MG 5.6 ± 1.5; 2.7 ± 0.8 mg/L, FEB2MG 1.5 ± 0.1. %; $1.1\% \pm 0.3$. All of these values in results were higher than normal in both groups, but there was no significant difference between the two groups. In U-UTI group, the mean of FEB2MG was significantly higher with VUR+(1.9 ± 0.7%; VUR+, 0.6 ± 0.2%; VUR- [$P<0.01$]).
Discussion: Elevated u-B2MG in KD children could indicate renal tubular damages not only systemic vasculitis, and the severity of tubular damages in KD patients could be equivalent to that in U-UTI patients.
Conclusion: Our results indicated that the renal tubular dysfunction in the pathogenesis of KD may occur as same levels as U-UTI.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-427 - Distal renal tubular acidosis presenting with an acute hypokalemic paralysis in an older child with severe vesicoureteral reflux and syringomyelia: A case report

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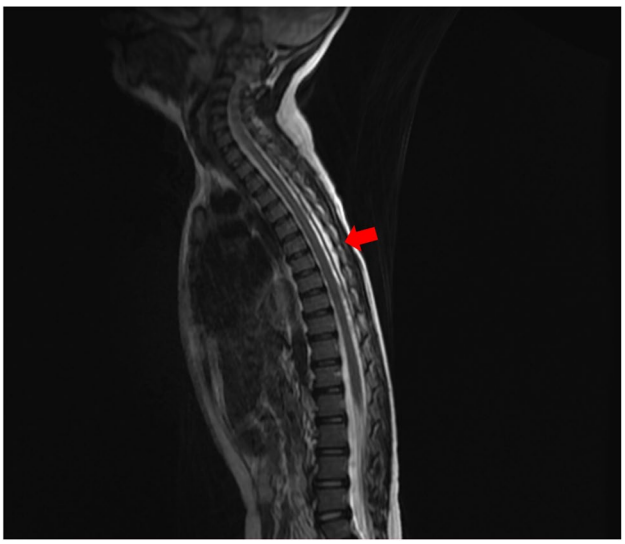
Background: Distal renal tubular acidosis (dRTA) is the most common type of renal tubular acidosis (RTA) in children. Pediatric dRTA is usually genetic and rarely occurs due to acquired issues such as obstructive uropathies, recurrent urinary tract infections (UTIs), and chronic kidney disease (CKD). Although persistent hypokalemia frequently occurs with dRTA, acute hypokalemic paralysis is not frequently reported, especially in older children.
Case presentation: An eight-year-old girl presented with an acute first episode of paralysis**.** A physical examination revealed normal vital signs, short stature consistent with her genetic potential, and decreased muscle strength of her upper and lower extremities. Preexisting conditions included stage 4 CKD due to recurrent UTIs, severe vesicoureteral reflux and bilateral hydronephrosis, neurogenic bladder, and multisegment thoracic syringomyelia. Her laboratory workup revealed hypokalemic, hyperchloremic metabolic acidosis with a normal anion gap. She also had a urine osmolal gap of 1.9 mOsmol/kg with a high urine pH. Intravenous potassium replacement resulted in a complete resolution of her paralysis. She was diagnosed with dRTA and discharged with oral bicarbonate and slow-release potassium supplementation.
Figure 1.



Sagittal T2-weighted whole spine magnetic resonance imagings (MRIs) of the patient indicating syringomyelia at T2–T7 level (arrow)
Conclusion: This case report highlights the importance of considering dRTA in the differential diagnosis of hypokalemic acute paralysis in children. Additionally, in children with neurogenic lower urinary tract dysfunction and recurrent UTIs, early diagnosis of spinal cord etiology is crucial to treat promptly, slow the progression of CKD, and prevent long-term complications such as RTA.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-428 - An unusual presentation of Dent disease associated with phenotypic findings of Bartter-like syndrome: A case report

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Introduction: Dent disease is an X-linked renal proximal tubular disorder, mainly caused by inactivating mutations of the CLCN5 gene. Bartter-like syndrome is a rare phenotypic finding in these patients.
Objective: To report the case of a boy with clinical presentation of Bartter-like syndrome, associated with proteinuria, hypercalciuria, nephrocalcinosis, hypophosphatemic rickets, and growth failure.
Description: A five-year-old boy was admitted due to short stature, low weight, vomit, and diarrhea. He was born at term, birth weight 3.566g, and has no family history of kidney disease or consanguinity. At admission, he was 91 cm tall (z-score -4,09), weight 11.2 kg (z-score -3,81), normal blood pressure (89 x 52mmHg). Laboratory tests showed: Bicarbonate 28 mEq/L, Chloride: 87mEq/L, Potassium 2.9 mg/dL, plasma renin 306.9 ng/mL and aldosterone 95.6 ng/dL (reference value: renin 2.8 to 39.9 ng/mL; aldosterone 1-19.0 ng/dL), Sodium 135 mEq/L, Calcium 10.4 mg/dL, Phosphate 2.2mg/dl, PTH 23.8 pg/mL, 25-hydroxy-vitamin-D 25ng/mL. Glomerular filtration rate 103.1 mL/m^2/1.73 m^2. Urinary calcium/creatinine ratio 2.17 mg/mg, proteinuria 1.3 g/24 hours, tubular reabsorption of phosphorus 73.7%. Renal ultrasound without abnormalities. X-ray showing cup-shaped bones with enlargement, generalized osteopenia, and delayed appearance of epiphyseal centers. Ophthalmologic and otorhinolaryngologic evaluation without abnormalities. Normal neurological development. Now he is ten-year-old, and a new generation sequencing test showed a stop codon monozygotic mutation in the CLCN5 gene, c. 1039C>T (p.Arg347*) associated with Dent's disease type 1. He is using enalapril 5mg/day, potassium citrate 1.5mEq/kg/day and potassium phosphate monohydrated 75mg/kg/day. For the last three months, he has begun growth hormone and grown up 6 cm. His electrolytes are stable, the GFR is 78.0mL/m^2/1.73 m^2, and the renal ultrasound showed nephrocalcinosis.
Discussion/ Conclusion: We reported an unusual clinical presentation of Dent disease with the coexistence of a Bartter-like syndrome phenotype, in which genetic test helped us elucidate the diagnosis.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-429 - Asymptomatic tubulointerstitial nephritis in sarcoidosis; a report of two young Japanese patients

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Background: Sarcoidosis is a rare granulomatous inflammatory disease of unknown etiology. There are two types of the diseases among children; pediatric-onset adult type sarcoidosis and early-onset

sarcoidosis/Blau syndrome which is caused by *NOD2* mutation. Although multiple tissues and organs, especially lungs, lymph nodes and eyes are affected, renal involvement is rare. Moreover, most reported cases of renal sarcoidosis in children manifested as acute renal injury or renal failure. We describe two cases of clinically asymptomatic tubulointerstitial nephritis in young Japanese patients with pediatric-onset adult type sarcoidosis.
Case presentation: Case 1; A 10-year-old Japanese girl with sudden onset bilateral granulomatous uveitis was diagnosed as sarcoidosis by elevated serum soluble interleukin-2 receptor, ocular lesion and non-caseating granuloma in parotid. A physical examination revealed no abnormalities besides severe obesity. Although her renal function was normal, we performed renal biopsy because urinary beta-2 microglobulin was slightly elevated. Non granulomatous tubulointerstitial nephritis was found in the kidney. After the initiation of treatment with 40 mg/day of oral prednisolone, urinary beta-2 microglobulin decreased rapidly. Case 2; A 14-year-old Japanese male patient with one month history of bilateral granulomatous uveitis was diagnosed as sarcoidosis by pathological findings in parotid and clinical features such as increased soluble interleukin-2 receptor and ocular lesions. Physical examination revealed no abnormalities. His serum creatinine level had been slightly elevated up to 1.11 mg/dL but did not meet any criteria for acute kidney injury. Due to an increase of urinary beta-2 microglobulin, renal biopsy was performed and granulomatous tubulointerstitial nephritis was observed. After the initiation of treatment with 40 mg/day of oral prednisolone, urinary beta-2 microglobulin decreased rapidly.
Conclusions: Our cases indicate the possible existence of "silent" tubulointerstitial nephritis in young patients with sarcoidosis. Measurement of urinary beta-2 microglobulin and renal biopsy are warranted for patients with sarcoidosis.

Tubulopathies and electrolyte disorders (including tubulointerstitial diseases)

P2-433 - Pediatric Primary Sjögren Syndrome Presenting With Extraglandular Features:A Case Report

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Primary Sjögren syndrome(pSS) is uncommon in children, predominantly affecting middle-aged women. Its rarity and atypical clinical manifestations pose a particular challenge to pediatrician in diagnosis. Here we report a case of a 12-year-old female patient initially presented with hypokalaemic paralysis and metabolic acidosis. She was misdiagnosed as renal tubular acidosis (RTA) in local hospital due to the absence of typical sicca syndrome symptoms such as *xerostomia or xerophthalmia.* After she was transferred to our department, labial gland and renal biopsies were performed owing to the positive antibodies (anti-SSA/SSB, ANA) together with tubular dysfunction. Pathological results revealed the lymphocytic infiltration within the tubulo-interstitium and salivary gland (focus score of $\geq$1 foci/4 mm^2), therefore the diagnosis of Sjogren's syndrome was established. Besides, her CT scanning,muscle enzyme profile as well as alanine aminotransferase level were abnormal. After the symptomatic treatment and addition of steroid, she improved gradually.During follow-up, the patient maintained on low-dose prednisone with persistent immunological abnormalities and tubular proteinuria despite normal renal function. To our knowledge this is the first report of a pediatric pSS patient with so many extraglandular organs involvement(kidney, lung, muscle and liver).This case indicates that the RTA in female teenagers could be the early manifestation of systemic autoimmune diseases.

Acute Kidney Injury (including CKRT)

P3-434 - Prevalence and outcome of Acute Kidney Injury (AKI) in Multi System Inflammatory Syndrome in Children (MIS-C)

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Objective: Multi System Inflammatory Syndrome in Children (MIS-C) led to serious and life-threatening complications including acute kidney injury. This study was done to find out the prevalence, severity and outcome of AKI in children with MIS-C
Methods: This prospective observational study was conducted in the department of Pediatric Nephrology, Bangladesh Shishu Hospital & Institute from November'2020 to October'2021. Total 22 children diagnosed according to WHO diagnostic criteria of MIS-C and all positive for COVID 19 antibody. KDIGO staging was done for AKI diagnosis. Patients were managed in Critical Care nephrology Unit with all supportive therapy along with dialysis and outcome was assessed.
Results: Age ranged from 4months to 11 year, M: F =2.14:1. Out of 22, renal involvement was found in 18% (n=4), 1 with membrano proliferative glomerulonephritis with complement C3 deposition and 3(13.6%) had AKI. All AKI cases were at KDIGO stage III and required dialysis. Mean value of CRP (300.3 gm/l), Ferritin (800 ng/ml), D dimer (9.76mg/l) and Pro calcitonin (12.5ng/ml) was markedly raised in AKI cohort compared to non AKI (82%). No significant difference regarding other organ system involvement had been seen between AKI and non AKI groups. Six children had co existing dengue infection 1 in AKI group and 5 in non AKI group. One case of MIS- C in a preexisting Dengue hemorrhagic fever grade III with AKI with coronary dilatation, hypotension and shock died. There was no mortality in non AKI group. Overall mortality 4.5%.
Conclusion: AKI prevalence in MIS-C was 18%. Need for dialysis was due to late presentation at AKI stage 3. C3 GN may be caused by COVID-19 infection. Fatal outcome was mostly due to hypotension, shock, cardiac complications and co existing Dengue haemorrhagic fever.
Keywords: acute kidney injury, COVID-19, MIS-C, children

Acute Kidney Injury (including CKRT)

P3-435 - Superior Mesenteric Artery Syndrome (SMAS): revisiting this rare condition as a cause of Acute Kidney Injury

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SMAS: is a rare disorder characterized by compression of the third, or transverse, portion of the duodenum between the aorta and the superior mesenteric artery (SMA) due to loss of the mesenteric fat pad that surrounds the SMA resulting in complete or partial duodenal obstruction. [1] It was first described in 1861 by Von Rokitansky.[1] Incidence is between 0.013-0.78%.[1]
We describe a 14 year old female with 3 days history of central abdominal pain, reduced intake, intractable bilious vomiting following significant weight loss due to food restriction for about a year. She developed severe azotemia, metabolic alkalosis and oliguria. Provisional diagnosis was Intestinal obstruction with Prerenal Acute Kidney Injury 2o dehydration. Investigations include Abdominal Xray/USS which did not show any surgical cause of

obstruction, infection screen was also normal. Non-contrast CT scan confirmed SMAS with duodenal compression at level of D3 and SMA take off angle of <25°, there was no abnormality of the renal system/vessels.
She was successfully managed conservatively. AKI resolved with Rehydration, SMAS with Total Parenteral nutrition, she was weaned onto Nasojejunal tube feeds and eventually oral feeds. Her weight improved and she was discharged after 4 weeks.
Any abnormality or debilitating condition causing severe weight loss can cause SMAS. Symptoms include feeling of fullness/bloating, nausea, bilious vomiting, mid abdominal crampy pain, weight loss.
Management involves reversing or removing the precipitating factor and is usually conservative, surgical intervention is indicated only when conservative measures are ineffective.
The outcome is excellent if diagnosed promptly and appropriate therapy given. Mortality can result from complications like dehydration, hypokalemia, oliguria/AKI mostly with delayed or missed diagnosis. Hence this case aims to raise awareness of this rare condition which requires high index of suspicion and can have excellent outcome if recognized early.

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Acute Kidney Injury (including CKRT)

P3-438 - Serum Cystatin C as early predictor of Acute Kidney Injury in preterm neonates with Respiratory Distress Syndrome

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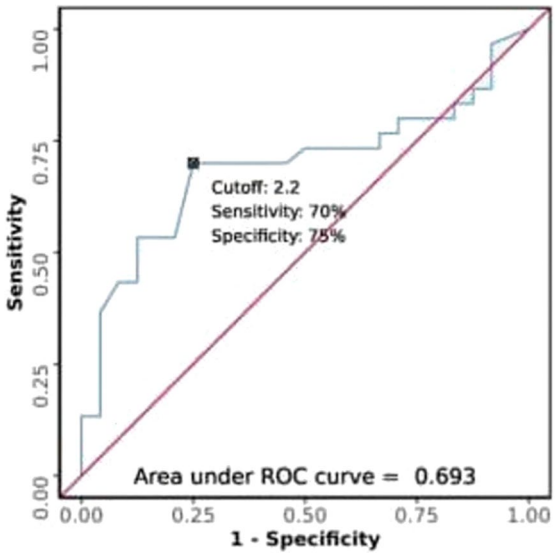
Context: Acute Kidney Injury (AKI) is associated with poor outcome in preterm neonates with Respiratory Distress Syndrome (RDS), leading to focus on novel biomarkers for early diagnosis.
Aim: To study diagnostic accuracy of serum Cystatin C(sCysC) in early prediction of AKI in preterm newborns with RDS.
Study setting and design: Prospective case control study in tertiary level teaching hospital in New Delhi (October 2019 - April 2021).
Methods: Total 90 preterms with gestation <37 weeks were enrolled and grouped as; case (n=60) including preterms with RDS and control (n=30) including healthy preterms. KDIGO classification was used for staging AKI. Serum Creatinine (sCr; JAFFE method) & sCysC levels (nephlometric method) were measured at day 1, 3 and 7.
Statistical Analysis: SPSS version 23
Results: Mean gestational age and weight in cases was 33.87 ± 1.78 weeks & 1.68 ± 0.40kg respectively compared to 35.10 ± 0.76 weeks & 2.01 ± 0.24kg in controls. Amongst cases, 32 (53.3%) developed AKI (stage 1- 43.3%, stage 2- 8.3%, stage 3- 1.7%) in comparison to 6(20%) in controls (all stage 1). Mean sCysC concentration (mg/l) in cases on day1,3,7 was 2.39±1.67,2.62±1.68, 3.07±2.33 respectively (reference lab value 0.55-1.15). Mean sCysC levels(mg/l) were highest in stage 3 AKI (4.68±2.82 in stage 1, 5.27±2.41 in stage 2, 7.00 in stage 3). Receiver operatic characteristics (ROC) for sCr and sCysC plotted on day1,3 and 7 to compare diagnostic performance of both. Area under curve was found to be 0.81 and 0.693 respectively (day 3). The sensitivity and specificity of sCysC on day 3 was 70% and 75% respectively (cut off 2.2mg/l) compared to 87% sensitivity and 62% specificity of sCr (cut off 0.8mg/dl).
Conclusion: Serum Cystatin C may be a good and reliable screening tool to predict AKI early in preterm neonates, in combination with sCr and other biomarkers.



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Acute Kidney Injury (including CKRT)

P3-440 - Acute kidney injury following multisystem inflammatory syndrome in children: A systematic review and meta-analysis

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Introduction: Multisystem inflammatory syndrome(MISC) has been described similar to Kawasaki disease in its profile, but temporally associated with COVID-19 and it is associated with multiorgan system involvement including acute kidney injury(AKI). This meta-analysis focuses on AKI in setting of MISC.
Methods
Data sources: We searched database from Medline, Google scholar and Embase till December 2021 utilizing following search strategy- "((((((acute kidney injury) OR (acute renal failure)) OR (renal failure)) AND (multisystem inflammatory syndrome)) OR (mis-c)) OR (pediatric multisystem inflammatory syndrome)) OR (pims covid)". We used Bejaut's plot, influential analysis and sensitivity analysis in case of unexplained heterogeneity.
Quality assessment: The quality of the included studies was assessed using the NHBL criterion.

Inclusion criterion: Studies meeting the following criterion were included in this systematic review: 1) articles on AKI in MISC; 2) studies providing AKI in MISC and in COVID 19 infection separately; 3) studies reporting outcomes such as mortality, renal replacement therapy, serum creatinine; length of hospital /ICU stay. Studies were excluded if they were case reports, case series with included patients<10, review articles, letters etc.
Results: A total of eleven articles were included in the quantitative synthesis. The study quality was variable. The pooled proportion of MISC children developing AKI was 19% (95% CI: 14%, 28%, I^2=80%, 11 studies). Three studies, staged AKI based on KDIGO criterion. The overall pooled proportion of MISC induced AKI patients requiring renal replacement therapy was 3% (95% CI: 1%; 11%; I^2=90, 5 studies), and overall mortality in the patients with MISC was 4%(95% CI:1%;14%). The odds of mortality in MISC patients with AKI was 4.68 times as compared to non AKI patients. Significant heterogeneity was present and we utilized various statistical tools such as Baujat's plot, influential analysis and leave one out analysis to address the heterogeneity.
Conclusion: MISC with AKI is associated with higher mortality.
Prospero: CRD42022306170

Acute Kidney Injury (including CKRT)

P3-441 - Acute kidney injury due to snakebites among the pediatric population in the state of Santa Catarina - Brazil

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Background: Acute Kidney Injury (AKI) is the main complication of snakebites in several species of snakes, most commonly associated with the Bothrops and Crotalus species in South and Central America. However, the incidence of these accidents and the behavior of venom in the pediatric population remains poorly described in the literature. This study was conducted to analyze the frequency of AKI and epidemiological characteristics of children victims of accidents caused by snakes Bothrops species.
Methods: All children aged 0-18 years who were victims of accidents with Bothrops snakes in the state of Santa Catarina-Brazil during the period from 2014 to 2020 were enrolled in the study. The AKI was diagnosed using the KDIGO 2012 guidelines.
Results: Most accidents registered occurred in males (73,85%) and the mean age was 12 ± 4.6 years**.** AKI was observed in 74 children (15.34%). According to the KDIGO criteria, 93,2 % of these children met stage 1, 5,4 % met stage 2, and 1,3 % met stage 3. Also, decreased urine output was observed in 8,46% of the patients. A total of 40.77% patients were hospitalized with a median time to initiate antivenom therapy of 3.6 hours. Among all children with AKI, 24,6% received nephrotoxic drugs during the hospital stay. No patient received dialysis therapy and all children progressed to cure.
Conclusion: Snakebite-induced AKI is a systemic complication that requires attention in younger patients because they concentrate large amounts of venom on low body surface area. This study showed high prevalence of AKI in the pediatric population and low severity and mortality rate, which is consistent with previous studies. Prompt administration of antivenom therapy and avoiding the use of nephrotoxic drugs are important measures to prevent kidney dysfunction secondary to snakebites.
Keywords: Snakebites; AKI; epidemiology

Acute Kidney Injury (including CKRT)

P3-442 - Global Burden and Mortality of Pediatric Acute Kidney Injury: A Systematic Review and Meta-analysis

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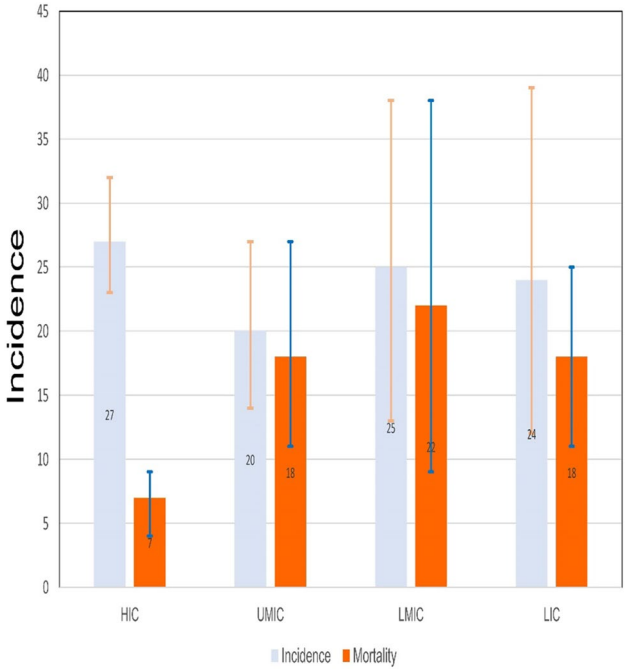
Introduction: There is limited literature with regards to the global burden of acute kidney injury (AKI) and associated mortality in children. It is crucial to systematically assess AKI epidemiology at a global level to allow appropriate health resource allocation and inform policymakers.
Methods: The protocol was registered with PROSPERO (CRD42021292618). Large cohort studies reporting the incidence of AKI using KDIGO criteria were considered eligible for this review. Three electronic databases (EMBASE, PubMed, and Web of Science) were searched for studies published after 2012. Search strategies were formulated using keywords related to acute kidney injury and children. The primary outcome was the global incidence of AKI. Secondary outcomes were incidence and AKI-associated mortality across various subgroups. Pooled estimates were generated using random-effect meta-analysis. The modified Hoy et al. tool was used for assessing the risk of bias.
Results: Our literature search yielded 10,906 records, of which 94 studies (with 202,694 participants) from 26 countries were eligible for systematic review. The global incidence of AKI in children regardless of the stage was 26% (95% confidence interval [CI] 22- 29). Whereas the incidence of severe AKI was 14% (11-16) in children. The incidence of AKI was 27% (23-32) in high-income countries (HIC), 20% (14-27) in upper-middle-income countries (UMIC), 25% (13-38) in low-middle-income countries (LMIC), and 24% (12-39) in low-income countries (LIC). AKI-associated mortality was observed in 11% (9-13) of children. The mortality rate was lowest at 7% (4-9) in HIC and highest at 18% (11-25) and 22% (9-38) in LIC and LMIC, respectively.
Conclusion: AKI was observed in one-quarter of the hospitalized children, and it is associated with an increased risk of mortality. LIC and LMIC had observed higher mortality rates despite a slightly lower burden of AKI.

Figure title: Variation in incidence and mortality as per various economic groups of countries



Acute Kidney Injury (including CKRT)

P3-443 - Acute kidney injury in Weil's disease: A case series of neglected tropical disease emerging during rainy season in Indonesia

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Leptospirosis is a prevalent zoonotic disease in developing countries especially emerges during rainy season. Mammals, mostly rodents, are reservoir of *Leptospira* which these pathogens remain in proximal tubules, excreted in urine, and infect humans through direct contact with mucous membrane. Multiple organ involvement, essentially kidney dysfunction, is characteristic of severe leptospiral infection which termed as Weil's disease. Adolescents tend to have more serious clinical manifestations compare to younger children. Here we discuss two adolescents (10 and 17-years old) with Weil's disease occurred during rainy season in Indonesia.
Both patients had chief complaint of low-grade fever less than a week. Severe knee pain, jaundice, and brownish urine were also the most prominent symptoms. There was history of playing in dirty water during rainy days. Physical examination revealed icteric sclera, discomfort in epigastric region, and skin rashes. Both patients had decrease of urine output confirmed by glomerular filtration rate decline which indicated acute kidney injury. Positive result of IgM *Leptospira* and polymerase chain reaction supported working diagnosis. Third-generation cephalosporin was administered since patients were considered as severe leptospiral infection. Full hydration with intravenous fluid was performed to improve renal functions and monitored every two days. Both patients had significant renal functions improvement after hydration and seven days of antibiotic treatment.
Therefore, this study highlights the importance of appropriate antibiotic, adequate supportive treatment, and kidney functions close monitoring in Weil's disease management.

Acute Kidney Injury (including CKRT)

P3-444 - Comparison of survival among continuous and prolonged intermittent Kidney replacement therapy in critically ill children

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Acute kidney injury in children in intensive care is often secondary to shock and multi-organ dysfunction syndrome. Continuous kidney replacement therapy (CKRT) has several disadvantages, including intensive nursing requirements, continuous anticoagulation, patient immobility and expensive equipment. Prolonged intermittent kidney replacement therapy (PIKRT) refers to intermittent kidney replacement therapy over an extended period. There is now evidence in favor of this therapy especially in adults, with few case series from pediatric literature.
Purpose: The aims of this study were to describe the demographic characteristics of critically ill children requiring CKRT and PIKRT at a pediatric intensive care unit (PICU) in a tertiary care center and to compare survival between them.
Methods: Retrospective single center study analyzing critically ill children admitted to PICU that required CKRT or PIKRT between January 2013 and January 2022. Between January 2013 and December 2019 all these children were treated with PIKRT (Fresenius 4008 or Genius) because CKRT machines were not available in our center, and between January 2019 and January 2022, with different modalities of CRRT (Fresenius multiFiltrate Acute Therapy System). Primary outcome was patient survival at 28 days after initiation of treatment.
Results: We analyzed data of 56 children, 42 on PIKRT and 14 on CKRT.Baseline characteristics of study patients are presented in Table 1. Survival at 28 days after initiation of treatment was similar in both groups (PIKRT 68%, CKRT 78% p=0.33) Overall, premature terminations had to be done in 12 patients for intractable hypotension or circuit clotting. Heparin free sessions were more frequently achieved in the PIKRT group (65 %) than in CKRT group (15%) p=0.001

Table 1 Baseline characteristics of study patients (Data are presented as mean with the standard deviation in parenthesis, n number of presentation)

Characteristic	All Patients (n = 56)	PIKRT (n = 42)	CKRT (n = 14)	P value
Age , years	8.9 (±5.6)	8.5(±5.7)	10(5±.0)	0.3
Female	33(58)	27 (64)	6(42)	0.2
Weight, (kg)	30(±18)	28.1(±18)	39 (±19)	0.06
Fluid overload >10% (%)		23 (54%)	2 (14)	0.01
PIM2 score at PICU admission	11.9 (±12.1)	9.8 (1±0.7)	18 (±14)	**0.053**
Underlying disease n (%)				
Malignancy (including bone marrow transplant)	20 (36%)	14 (33)	6 (43)	0.8
Liver disease/ transplant	21 (38%)	14 (33)	7 (50)	
Cardiac disease/Transplant	8 (14%)	7 (17)	1 (7)	
Other	7 (12%)	7 (17)	0	
Primary reasons for ICU admission, n (%)				**0.04**
Sepsis	9 (41%)	16 (38)	4 (28)	
Cardiac failure	8 (36%)	17 (40)	3 (21)	
Metabolic abnormalities	5 (23%)	9 (22)	7 (50)	
On vasoactive drugs at RRT initiation, n (%)	42 (75)	32 (80)	10 (71)	0.7
Mechanical ventilation n (%)	50 (89)	38 (90)	12 (86)	0.6
Multiple organ failure MODS [≥2 organ failure], n (%)	36(64)	27 (64)	9 (65)	1.0
KRT parameters				
duration(days)		4.5(±2.9)	2(±1.2)	
treatment duration hs		6.3 (0.8)	-	
Modality				
CVVHD			7	
CVVHDF			1	
CVVH			6	
Heparin anticoagulation, n (%)	27(48)	15 (35)	12(85)	**0.001**
Survival at 28 days after initiation of treatment n (%)	37 (66)	26(62)	11(78)	0.33
Patients prematurely discontinued for complications n (%)	12 (21)	10 (23)	2 (14)	0.7

Conclusion: PIKRT is a viable alternative to traditional CKRT for critically ill children although prospective studies directly comparing different modalities are required.

Acute Kidney Injury (including CKRT)

P3-446 - Renal replacement therapy (RRT) in children undergoing allogenic hematopoietic stem cell transplantation (HSCT)

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Introduction: The aim of the study was single center retrospective data analysis of 12 children who required RRT due to acute kidney injury (AKI)in group of 211 patients treated with allogenic HSCTin Children's University Hospital of Cracow from Jan 2006 till Dec 2021.
Methods: Indications for HSCT and conditioning regimen, transplant specifics (type of donor, HLA matching-status, GVHD prophylaxis, number or HSCTs) and clinical data concerning RRT (the medication used, indication for RRT, dialysis data, outcome) were reviewed. Indications for HSCT were hemato-oncological disorders, in 5 cases it was due to recurrence of oncologic disease. The conditioning regiments were accordant to current recommendation.
Results: All but one children had normal eGFR before HSCT (one patient CKD stage 3) and in his case the CRRT was planned as a preparation for HSCT. RRT was performed in 5,4 % of all HSCT recipients, only in 1 infant - peritoneal dialysis was chosen, for the others - CRRT (HDF). The indication for RRT was: hypervolemia (50%), AKI (33%), MOF (8,3%), prevention (8,3%) in the child with CKD. In all children except 2 cases – RRT was done within 100 days after the date of HSCT. The average duration time of dialysis was: 15,6 days. The coexisting comorbidity (apart from AKI) were present in all children: GvHD in different stages in all pts, sepsis (41,7%), CMV infection (33,3%) and other diseases. 2/3 of children died up to 2 months after RRT start, 1 pts died in later period with CKD. The only child with CKD at the moment of HSCT preserved stable CKD stage. In children without AKI and RRT - the mortality was 18%.
Conclusion: RRT is rarely performed in children with AKI after allogenic HSCT but the necessity of dialysis is a great risk factor for death in this group of patients.

Acute Kidney Injury (including CKRT)

P3-447 - Acute kidney injury associated with COVID-19 and Multisystem Inflammatory Syndrome in Children (MIS-C)

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Objectives: Data on the characteristics of acute kidney injury (AKI) in pediatric COVID-19 and MIS-C are limited. We aimed to define the frequency, associated factors and early outcome of AKI in COVID-19 and MIS-C.
Methods: Hospitalized patients ≤18 years of age with confirmed COVID-19 or MIS-C at a tertiary center, between March 2020 - December 2021 were enrolled. AKI was defined and staged according to KDIGO criteria. The characteristics of AKI in the COVID-19 group were investigated in moderate, severe and critically ill patients; outpatients and mild cases who do not have shortness of breath, dyspnea, or abnormal chest imaging were excluded.
Results: The study included 66 moderate-severe-critically ill patients with COVID-19 (9.71 ± 6.08 years) and 111 MIS-C patients (8.72 ± 4.72 years). The frequency of AKI was 22.7% in COVID-19 and 15.3% in MIS-C; among them AKI was present on admission in 73.3% and 88.2% of COVID-19 and MIS-C groups, respectively. In univariate analyzes, presentation with vomiting/diarrhea, high LDH, D-dimer, troponin and procalcitonin on admission were associated with AKI in COVID-19 patients; whereas older age, low albumin, hemoglobin, thrombocyte, and high CRP, procalcitonin, ferritin, D-dimer, troponin, and BNP levels and low ejection fraction on echocardiography on admission were associated with AKI in MIS-C group. Length of hospital stay was significantly longer in both COVID-19 and MIS-C patients with AKI, compared to those without AKI. Mortality was 9.1% in COVID-19 group; there was no mortality in MIS-C patients. AKI was associated with mortality in COVID-19 patients (p=0.021). Serum creatinine returned to normal level in 96% of survivors before discharge.
Conclusion: AKI was seen in 15% of moderate-severe-critically ill COVID-19 group and 23% of MIS-C; it was associated with mortality in COVID-19. Clinical and laboratory parameters associated with AKI were different in COVID-19 and MIS-C. Early outcome was excellent among survivors.

Acute Kidney Injury (including CKRT)

P3-448 - Acute kidney injury (AKI) in patients with "Hypoplastic Left Heart syndrome" (HLHS) undergoing Norwood-sano (NS) surgery at a reference hospital in São Paulo (Brazil).

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Objective: To describe the epidemiological profile and the factors associated with AKI in the postoperative (PO) HLHS patients.
Methods: Analysis of a retrospective cohort of patients with HLHS undergoing NS in the period from 2019 to 2020.
Results: A total of 38 patients were evaluated, being 58% male. The average age was 9 days (2 - 55) and the average weight was 3.08 kg (1.82 - 4.10). The average time of cardiopulmonary by-pass (CPB) was 189 min (106 - 375). The prevalence of AKI was 86% and 75% required renal replacement therapy (RRT). CPB > 180 min was correlated with progression to AKI. The Peritoneal dialysis (PD) was the most used RRT (22/24 patients). Fluid overload (> 10%) was noted in 76% of patients, being the main indication for RRT. Furosemide (> 4 mg/kg/day) was used in 73% of patients. The initial time of PD installation varied from 0 to 3 days, with 62% starting in the immediate PO period. The average time of PD was 13,25 days (3 - 61). Peritonitis was detected in one patient. Ten patients underwent extracorporeal membrane oxygenation (ECMO) and required RRT. The survival time was 71% and after the ICU discharge, all patients had a recovery of theirs baseline renal function.
Conclusion: AKI in patients with HLHS undergoing NS is a frequent complication and a risk factor for morbidity and mortality. The PD is the first line TSR, being effective and safe. Due to the surgical complexity, risk factors and limitations of the use of traditional biomarkers in AKI, we consider the need for an early onset of PD. Periodic follow-up of the renal function and other complications is recommended.

Acute Kidney Injury (including CKRT)

P3-450 - The association between intravenous solution- induced hyperchloremia, metabolic acidosis and new or progressive acute kidney injury among pediatric patients with Diabetic Ketoacidosis. A retrospective cohort study.

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Background: Diabetic Ketoacidosis requires large and immediate fluid resuscitation. Excessive administration of high chloride containing IV fluids can cause hyperchloremia. Currently, there is scarcity of data associating hyperchloremia with acute kidney injury and prolonged metabolic acidosis among children with DKA.
Objective: To investigate the association between intravenous solution- induced hyperchloremia, metabolic acidosis and acute kidney injury among DKA patients
Methods: This is a retrospective cohort study among cases of Diabetic Ketoacidosis. The serum chloride level were reviewed, the total chloride infused was computed and compared per time interval by repeated measures ANOVA. Hyperchloremic cases were determined and were analyzed for the occurrence and association with acute kidney injury using Fisher exact test. The serum chloride, total chloride infused, total fluid input and urine output among those with and without AKI were evaluated. The length of DKA resolution was compared among the hyperchloremic and nonhyperchloremic group.
Results: There were 280 cases of DKA but only 167 were eligible. 158 (94.6%) of these developed hyperchloremia and 36 (21%) had acute kidney injury. The association between hyperchloremia and acute kidney is not statistically significant (P=0.21) but a significant decreased in urine output among the cases was proven (P=0.008). The length of DKA resolution by closure of anion gap has an average of 21.29 (±13.95) hours while the rise of pH has 25.51 (±14.77) hours and 29.7 (±14.89) hours for HCO3. Hyperchloremic group has longer duration of DKA resolution by pH (P= 0.0281) and bicarbonate (P= 0.0080) while no statistical difference was noted for the closure of anion gap between the two groups.
Conclusion and Recommendation: The study showed that hyperchloremia (94%) is common during fluid resuscitation. It causes prolonged metabolic acidosis and decreased urine output which can lead to acute kidney injury. A randomized controlled trial may be done to strengthen these observations.

Acute Kidney Injury (including CKRT)

P3-451 - Improvement of diagnostic performance for prediction of acute kidney injury by incorporating additional risk factors into the renal angina index

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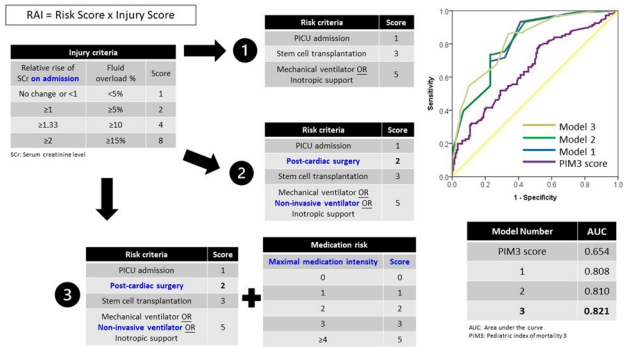
Introduction: Renal angina index (RAI) is a useful clinical tool for determining the risk of acute kidney injury (AKI) among critically ill children. Recent studies have identified additional risk factors not included in the RAI that may predispose children to AKI development.
Method: A prospective study on AKI and electrolyte disturbances epidemiology was conducted from 6/2020 to 6/2021 on children aged 1 month to 18 years old admitted to the Paediatric Intensive Care Unit (PICU) of the Hong Kong Children's Hospital. We determined the relative risk (RR) of potential risk factors for AKI development and evaluated if incorporating these additional factors into the RAI model could improve its diagnostic performance. AKI was defined using the KDIGO criteria. Medication intensity was defined as the number of concomitant medication exposure.
Results: Altogether 254 episodes of admission were enrolled for analysis. 58.3% of children were male with a median (interquartile range) age of 4.9 (9.6) years old. The AKI incidence was 41.7%. Apart from factors that already included in the RAI, additional factors including post-cardiac operation (RR: 1.36 [1.00, 1.85]), non-invasive ventilatory support (RR: 1.72 [1.26, 2.35]), PIM3 score (RR: 1.05 [1.02, 1.08]), nephrotoxic medication exposure (RR: 1.94 [1.29, 2.92]), total dose of nephrotoxic medication (RR: 1.01 [1.00, 1.01]) and maximal medication intensity (RR: 1.15 [1.04, 1.28]) were identified. The incorporation of post-cardiac surgery, use of non-invasive ventilation and maximal

medication intensity yielded the best area under the curve (AUC) for predicting AKI during PICU stay (Figure 1). Model 3 also performed the best for prediction of AKI on Day 2 (AUC: 0.75) and Day 3 (AUC: 0.72) of admission.

Conclusion: Post-cardiac surgery, requirement of non-invasive ventilation and nephrotoxic medication exposure were important risk factors for AKI development among critically ill children. Incorporation of these factors into the RAI model may enhance its predictive performance.



Acute Kidney Injury (including CKRT)

P3-452 - Natural history of acute kidney injury and acute kidney disease among critically ill children

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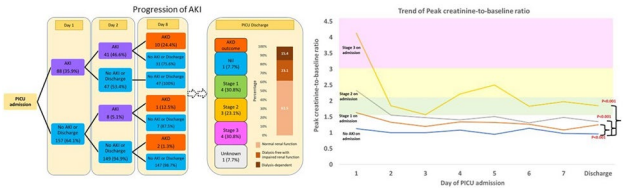
Introduction: The natural history of AKI and its progression to acute kidney disease (AKD) provide important prognostic information for children with AKI. We described the progression and outcomes of AKI among children admitted to the Paediatric Intensive Care Unit (PICU) of the Hong Kong Children's Hospital.

Methods: A prospective study on AKI epidemiology was conducted from 6/2020 to 6/2021 on children aged 1 month to 18 years old admitted to our PICU. AKI was defined using the KDIGO criteria, and AKD was defined as AKI lasting for >7 days.

Results: Altogether 254 episodes of admission were analyzed. Male accounted for 58.3% and the median (interquartile range) age was 4.9 (9.6) years old. The overall incidence of AKI was 41.7% (Stage 1: 18.5%; Stage 2: 14.2%; Stage 3: 9.1%) and AKD developed in 12.3% of children with AKI (Figure 1). 62.9% of children attained the highest AKI stage on day 1 of admission. Children with AKI were mostly non-oliguric with the median urine output being 2.8 (1.9) ml/kg/hour. The median duration of AKI was 2 (3) days and 33.3% of children with AKI had their serum creatinine level returning to baseline level. Acute dialysis was required among 3.5% of children. Initial AKI staging ($p<0.001$), the number ($p=0.004$) and intensity ($p=0.001$) of nephrotoxic medications exposure both determined AKI progression (Figure 1). Upon PICU discharge, AKI persisted in 18.0% of patients and 1.6% of them remained dialysis-dependent. Both AKI staging ($p<0.001$) and AKD ($p=0.026$) were associated with worse stage AKI upon discharge. AKI was associated with longer PICU stay ($p<0.001$) and higher PICU mortality ($p<0.001$).

Conclusion: AKI was common among critically ill children. A significant proportion of children with AKI developed AKD and persistent AKI upon discharge. A higher AKI stage and longer AKI duration were associated with worse renal outcome at PICU discharge.



Acute Kidney Injury (including CKRT)

P3-453 - Acute kidney injury in relation to nephrotoxic medication use among critically ill children in the paediatric intensive care unit (PICU)

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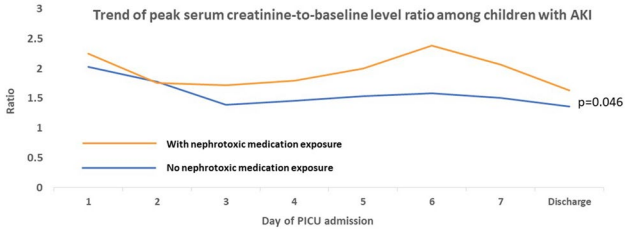
Background: Critically ill children are vulnerable to acute kidney injury (AKI) and are often exposed to multiple nephrotoxic medications. We presented the result of a prospective study on the potential association between nephrotoxic medications and the risk of AKI in children admitted to PICU of Hong Kong Children's Hospital.

Method: Patients aged > 1month to ≤ 18 years old were recruited from 6/2020 to 6/2021. The medication records from 14 days prior to PICU admission to PICU discharge were reviewed by an independent pharmacist to determine the number and doses of nephrotoxic medication exposure in relation to the development of AKI. Medication intensity was defined as the number of concomitant nephrotoxic medications.

Findings: Altogether 254 admissions fulfilling the study criteria were identified. The incidence of AKI was 41.7%. 68.9% of the patients were exposed to ≥1 of the 45 nephrotoxic medications. Nephrotoxic medication exposure (relative risk [RR]: 1.94 [1.29, 2.92]), total nephrotoxic medication dose (RR: 1.01 [1.00, 1.01]) and maximal medication intensity (RR: 1.15 [1.04, 1.28]) were all identified as risk factors for AKI development. The risk of AKI markedly increased when the maximal medication intensity (RR: 1.84 [1.23, 2.75]) was ≥4. During their PICU stay, children with AKI received a higher number ($p<0.01$), total dose ($p<0.01$) and maximal medication intensity ($p<0.01$) of nephrotoxic medications. A persistently higher serum creatinine level was also observed among children with AKI and nephrotoxic medication exposure ($p=0.046$) (Figure 1). Furosemide, vancomycin and spironolactone were the three medications with the highest total administered doses, but forscarnet, ganciclovir and cyclosporin A were the three medications with highest median number of doses and treatment days per patient.

Conclusion: Nephrotoxic medication exposure significantly increased the risk of AKI development among critically ill children. Both the number of medications, the total doses and medication intensity were associated with a worse renal outcome.

Nephrotoxic medication risk	AKI	No AKI	Relative risk (95% CI)
Ever received nephrotoxic medication	86 (49.1%)	20 (25.3%)	1.94 (1.29, 2.92)
Maximal medication intensity	1.5±1.6	1.1±1.1	1.15 (1.04, 1.28)
0 (Reference)	40 (40.8%)	58 (59.2%)	---
1	16 (30.2%)	37 (69.8%)	0.74 (0.46, 1.19)
2	29 (44.6%)	36 (55.4%)	1.09 (0.76, 1.57)
3	12 (46.2%)	14 (53.8%)	1.13 (0.70, 1.83)
≥4	9 (75%)	3 (25%)	1.84 (1.23, 2.75)
Total nephrotoxic medication dose	21.7±32.8	11.4±23.6	1.01 (1.00, 1.01)



Acute Kidney Injury (including CKRT)

P3-454 - Incidence, Risk Factors and Outcome of Acute Kidney Injury (AKI) in Children with Nephrotic Syndrome

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Children with nephrotic syndrome (NS) develop a variety of acute complications that can be serious and life-threatening, including infections, hypovolemia, venous thromboembolism (VTE), and acute kidney injury (AKI). There are number of potential risk factors for the development of AKI, including intravascular volume depletion, infection and exposure to nephrotoxic medication. AKI is associated with adverse outcomes in hospitalized children and can also progress to chronic kidney disease (CKD) and even death. Objectives of this study were to determine the incidence, risk factors and short term outcome of acute kidney injury (AKI) in children with nephrotic syndrome in the department of Pediatric Nephrology (in-patient department) Bangabandhu Sheikh Mujib Medical University. Total 144 patients aged between 1-18 years with nephrotic syndrome admitted in the in-patient department of Paediatric Nephrology fulfilling the inclusion criteria were enrolled for this study. In this study, serial serum creatinine was measured during hospital stay. When AKI was identified, risk factors were compared with non AKI group. Staging was done according to KDIGO guideline. The children with AKI were observed for outcome by measuring serial S. Creatinine at 15 days and monthly for 3 months. Out of 144 nephrotic syndrome children 18 patients developed AKI (12.5 %). Pneumonia (OR, 1.116; 95% CI, 0.62 to 2.842; p=0.033), cyclosporine (OR, 1.047; 95% CI, 1.003 to 2.814; p=0.036), tacrolimus (OR, 1.022; 95% CI, 1.001 to 2.535; p=0.019) were significantly associated with AKI in children with NS. After 3 months, 10(71.4%) patients got complete recovery and 2(14.28%) patients developed CKD. So, this study highlights the need to identify risk factors of AKI among nephrotic children and strategies need to be taken to reduce the morbidity and mortality of them.

Acute Kidney Injury (including CKRT)

P3-455 - Furosemide stress test to predict AKI progression in critically-ill children

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Background: Furosemide stress test (FST) is a novel functional biomarker for predicting severe acute kidney injury (AKI). As there are no prospective pediatric studies, we aimed to examine the role of FST in predicting AKI progression over 7 days in critically-ill children.
Methods: All children 3 months to 18 years of age admitted to the intensive care (ICU) or high dependency unit (HDU) of a tertiary care hospital from Nov 2019 to July 2021 were screened for eligibility. Patients who developed AKI stage 1 or 2 (KDIGO urine output or serum creatinine criteria) within seven days of admission underwent FST (intravenous furosemide at 1 mg/kg in naïve and 1.5 mg/kg in exposed) after catheterisation and urine output was measured hourly for the next six hours; output >2 ml/kg within the first two-hours was deemed furosemide responsive. Other biomarkers like plasma neutrophil gelatinase-associated lipocalin (NGAL) and proenkephalin (PENK) were also evaluated in these patients.
Results: Of the 480 admitted patients, 51 developed AKI stage 1 or 2 within seven days of admission and underwent FST. Twelve patients (23.5%) developed stage 3 AKI within seven days of FST, 9 (17.6%) of whom required kidney replacement therapy (KRT). FST emerged as a good biomarker for predicting stage 3 AKI and need for KRT with area under the curve (AUC) being 0.92 ± 0.05 (95% CI 0.82-1.0; p<0.0001) and 0.96 ± 0.03 (95% CI 0.9-1.0; p<0.0001), respectively. The corresponding AUC for NGAL and PENK were 0.75 ± 0.08 (95% CI 0.59-0.91; p 0.009) and 0.79 ± 0.08 (95% CI 0.64-0.94; p 0.003), respectively.
Conclusions: Furosemide stress test is a simple, inexpensive and robust biomarker for predicting stage 3 AKI and KRT need in critically-ill children; larger prospective studies are recommended before its routine clinical implementation.

Acute Kidney Injury (including CKRT)

P3-456 - Risk factors and a prediction score were evaluated for early detection of acute kidney injury caused by dengue viral infection in children

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Risk factors and a prediction score for acute kidney injury caused by dengue viral infection in children

Introduction: Acute kidney injury (AKI) in children with dengue viral infection (DVI) is one of a serious complication. Although, the AKI definitions have evolved, few studies have been reported the incidence and risk factor of AKI caused by DVI, particularly in children. No studies have also developed clinical predictor scores for early detection of AKI caused by DVI.
Objective: To study the risk factors and develop a prediction score for AKI caused by DVI in children
Material and methods: This study based on a single-center retrospective cohort of children admitted to our large tertiary care hospital during 5 years. AKI was defined according to Improving Global Outcomes (KDIGO) and pediatric RIFLE (pRIFLE) classification. All parameters were collected upon admission. Multivariable logistic regression was used to identify the strongest predictors. Developed clinical scoring model was calculated from logistic coefficient.
Result: A total of 572 patients were included. Of these, 98 patients (17.1%) had AKI by KDIGO classification, and 36 patients (6.3%) had AKI by pRIFLE classification. Six independent predictors for AKI were identified; hematocrit levels ≥ 40% (OR: 7.2; p <0.001), severe dengue infection (OR: 5.7; p <0.001), BMI ≥ 25 kg/m2 (OR: 8.2; p=0.006), leucocyte counts ≤ 4,000 cells/mm^3(OR: 3.9; p =0.003), platelet counts ≤ 100,000 cells/mm^3(OR: 17.9; p <0.001), and serum sodium level < 135 mmol/L (OR: 2.8; p =0.004). The cut-off score of ≥ 3 points had the optimal

discriminative power to distinguish between those with versus without AKI in dengue infection, with sensitivity of 92.9% and specificity of 77.1%.
Conclusion: Our prediction score is helpful for early detection of AKI caused by DVI in children, with a good performance and easily obtainable information.

Acute Kidney Injury (including CKRT)

P3-457 - Gravity assisted Continuous Flow Peritoneal Dialysis (CFPD) technique use in Acute Kidney Injury in children

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Background: One of the disadvantages of PD use for AKI is the low ultrafiltration and clearances compared to extracorporeal techniques. In a previous study we demonstrated increased ultrafiltration and clearances using CFPD in children with AKI. The technique was however expensive because of high volume pumps needed to circulate fluid.
Aim: To develop a technique for doing CFPD in children using cost effective equipment and using gravity to circulate fluid through the abdomen. To compare this technique to conventional peritoneal dialysis (PD)
Method: First an in vitro study was performed to design and test the hydraulics of such a system. Fifteen children with acute AKI requiring dialysis were recruited from our PICU. Two PD catheters were inserted at the bedside into each patient. Each patient received sequentially both conventional PD and CFPD in a randomised order. After initial filling, dialysate flow rate (50ml/1.73 m2 per minute) was maintained. Primary outcome were functionality and complications of the system and modalities were compared regarding ultrafiltration, clearances. Paired t test were used to compare these outcome.
Results: Mean age 8 Months(range 0,2-14), weight 6,3 kg (2,3-14). The system was easy and quick to set up. The system functioned well with minimal complications. Ultrafiltration achieved was approximately 4 times higher(p=0,003) with CFPD and clearances were doubled (p=0,001).
Conclusion: Gravity assisted CFPD is a cheap and effective way to augment ultrafiltration and clearances in peritoneal dialysis in children with AKI

Acute Kidney Injury (including CKRT)

P3-459 - Prevalence and outcome of AKI in children with Lassa fever in a tertiary Centre, Nigeria

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Background: Lassa fever causes AKI of varying severity in infected children, however, there has been little focus on this seemingly rising scourge.
Aim: To determine the prevalence and outcome of AKI in children with Lassa fever
Methodology: A retrospective study of Lassa fever in children diagnosed with RT-PCR at the Federal Medical Center, Owo. AKI was defined using the KDIGO criteria.
Results: A total of 81 children with Lassa fever were recruited in this study, 50.6% were males, with a mean age of 8.76±4.82 years. Fifty-eight percent (58.0%) had AKI, of which 29.0%, 14.8%,6.0% had stages 1, 2 and 3 KDIGO AKI respectively. More males (52.2%) had AKI while 19.1% had hemodialysis. Case fatality rate was 8.6% while 91.4% were discharged. All of the deaths recorded (100.0%) were in those with AKI stages 2 and 3. The mean duration of hospital stay for AKI patients was 17.87±9.73 days.
Conclusion: AKI is relatively common in children with Lassa fever, mortality occurs in patients with stages 2 and 3 AKI. More studies are needed on the risk factors for death, preventions and treatment of AKI in patients with Lassa fever.
Keywords: Acute Kidney Injury; Kidney Disease Improving Global Outcomes; Paediatric Lassa fever; Outcome.

Acute Kidney Injury (including CKRT)

P3-460 - Predictors of mortality and long-term outcomes of paediatric acute kidney injury in a resource limited setting

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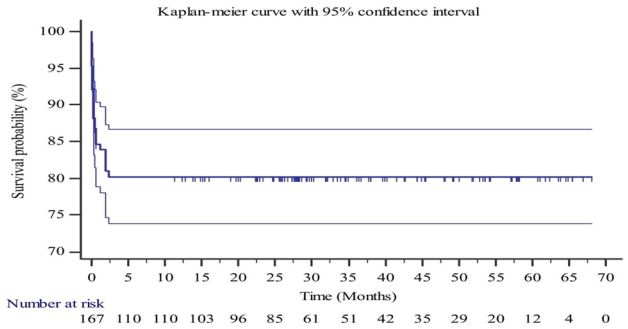
Background: Acute kidney injury (AKI) remains a leading cause of morbidity and mortality globally with resource-limited settings bearing a disproportionate share of the burden. This study looks at the predictors of mortality and long-term-outcomes in children with AKI in a resource-limited-setting.
Methods: This was a prospective study of children with AKI admitted between October 2014 and November 2019. AKI was diagnosed using the 2012 Kidney Disease Improving Global Outcomes definition. We assessed the aetiology, predictors of in-hospital mortality, and two-year survival of children with AKI in a mission hospital in South-West Nigeria.
Results: Of the 201 children with AKI, only 169 had a complete dataset. The median (interquartile range) age was 6 (3 to 12) and the male preponderance of 111 (65.7%) was largely from lower socioeconomic class (110; 65.1%). The peak age of incidence for AKI was aged 1 to 5 years (65; 38.5%). Twenty (11.2%) had kidney replacement therapy.

Sepsis was the most common cause of AKI (26.6%), followed by malaria (15.4%) and nephrotic syndrome (14.8%). Fever (72.8%) was the most common presenting symptom, followed by pallor (52.1%) and vomiting (45.6%). Thirty-two (27.8%) had elevated blood pressure. The clinical features, mean estimated glomerular filtration rate, and electrolytes except serum sodium were comparable between those who died and those discharged home. In-hospital mortality, 14.8%, 29 children were lost to follow-up while 7 died at follow-up, giving a cumulative mortality rate of 22.9% (32/140). The Kaplan-Meier survival curve shows a probability of survival of 80% (95% CI 74 to 87%) after an AKI.



On Cox proportional-hazards analysis, the absence of breathlessness (HR 2.537, 95% CI 1.210 to 5.317) and the absence of hyponatremia (HR 2.914, 95% CI 1.343 to 6.324) were factors associated with increased survival.

Conclusion: AKI in resource limited settings carries a high mortality rate with presenting breathlessness and hyponatraemia predictive of poor outcomes.

Acute Kidney Injury (including CKRT)

P3-461 - A rare cause of acute tubulointerstitial nephritis in a 16.5-year-old boy

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Introduction: Acute tubulointerstitial nephritis (ATN) is most often induced by drug therapy. It can be also caused by rare diseases like IgG4-related nephropathy.

Materials and methods: A 16.5-year-old boy with recurrent fever for last 4 months, weight loss and deteriorating kidney function was admitted to our department. At admission he was afebrile, with fibrotic papules on limbs, increased inflammatory activity (C-reactive protein [CRP] 8.9 mg/l), serum creatinine 1.69 mg/dl, creatinine clearance 48 ml/min/1.73m^2, cystatin C 1.47 mg/dl, cystatin C clearance 55 ml/min/1.73m^2, glomerulotubular proteinuria 1.1 g/24h, increased serum amyloid A (668 mg/l), IgA (2.1 g/l), IgM (1.78 g/l) and IgG4 (2.97 g/l). Due to increased CRP and dilatated left coronary artery in echocardiography a suspicion of pediatric inflammatory multisystem syndrome was made, however, the patient had no COVID history. Intravenous immunoglobulins, low-dose methylprednisolone (32 mg/24h) and Anakinra did not reduce the frequency of fevers nor improved kidney function. Increased IgG4 levels (3.18 g/l) indicated IgG4-related disease. The skin biopsy revealed paraepidermoid epithelium with hyperkeratosis. The kidney biopsy showed polymorphic tubular inflammatory infiltration and presence of IgG4 and CD138+ cells - indicative of IgG4-related disease. The treatment was intensified, high-dose methylprednisolone and mycophenolate mofetil (MMF) improved kidney function (serum creatinine 0.7 mg/dl, urinary protein-to-creatinine ratio 0.22 mg/mg), decreased CRP (0.2 mg/dl) and reduced IgG4 (2.77 g/l) levels. After 1 month the patient had normal kidney function and CRP 0.1 mg/dl. The therapy with low-dose prednisone and MMF was continued. After 3 months creatinine was 0.86 mg/dl and urinalysis showed no abnormalities.

Discussion and conclusions: IgG4-related disease is a multiorgan fibroinflammatory condition that can mimic PIMS and vasculitis syndromes or cause ATN, as in our case. The diagnosis is based on clinical manifestation, laboratory findings and renal biopsy. Intensive anti-inflammatory and immunosuppressive treatment may cause fast improvement and normalization of IgG4 levels.

Acute Kidney Injury (including CKRT)

P3-464 - Early detection of severe acute kidney injury by urinary Neutrophil Gelatinase-associated Lipocalin in critically ill children

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Background: Acute kidney injury (AKI) is independently associated with worsened morbidity and increased mortality in critically ill children in the pediatric intensive care unit (PICU). Till date serum creatinine (SCr) is the gold standard for AKI detection but it may not rise until 25-50% of kidney function has been lost which increases morbidity and mortality. So, new biomarker is needed for early detection of severe AKI, like urinary neutrophil gelatinase-associated lipocalin (uNGAL).

Objective: To evaluate the ability of uNGAL for early detection of severe AKI in critically ill children admitted in PICU.

Materials and Method: This prospective observational study was carried out on 90 PICU patients of Chittagong Medical College Hospital, from December 2020 to November 2021. Urine was collected for uNGAL on admission (Day 0) and blood samples on Day 0 (D_0), Day3 (D_3) and Day7 (D_7) for serum creatinine (SCr).

Results: Among 90 children, 26 (28.9%) develop AKI on day 3. The median uNGAL level was 182.85 ng/ml in children with severe AKI compared to 44.29 ng/ml in those without severe AKI (AKI group and non AKI group). Day 0 uNGAL level can detect Day 3 severe AKI [area under the curve (AUC) = 0.945, 95% confidence interval (CI) 0.867–1.0]. To discriminate severe and without severe AKI, the best cutoff point for uNGAL was 102.70 ng/ml, with a corresponding sensitivity of 96.15%, specificity of 98.44%, positive predictive value 96.15%, negative predictive value 98.44% and diagnostic accuracy 97.78%.

Conclusion: uNGAL can detect severe AKI earlier than SCr in critically ill children of PICU

Acute Kidney Injury (including CKRT)

P3-465 - Severe acute kidney injury and thrombotic microangiopathy following Sri Lankan Hypnale spp. envenoming: early plasma paresis as a potential therapy

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Introduction: Acute kidney injury (AKI) is a serious clinical manifestation of the Sri Lankan hump nosed pit viper (Hypnale spp.) bites. Thrombotic microangiopathy (TMA) is increasingly recognized in association with AKI in cases of Hypnale spp envenomation.
Case History: A five year old boy presented with severe acute kidney injury following hump nosed pit viper bite. He was born with a single functioning right kidney and renal functions has been normal until this incident. He was bitten on the dorsum of the right foot with local envenomation features. He was anuric on admission with serum creatinine of 315 µmol/l. The blood picture (BP) revealed the evidence of microangiopathic haemolytic anaemia (MAHA) with haemoglobin of 6.7 g/dl. The first session of haemodialysis was conducted on the day two of admission. He was transfused during the dialysis. Due to the evidence of MAHA and severe haemolysis with low platelet count (< 30000/l), the patient was started on therapeutic plasma paresis on day 3. He underwent seven consecutive cycles of plasma paresis until platelet count raised > 100000/l and settlement of MAHA. The requirement of dialysis has become less and kidney functions improved with settlement of MAHA. The child has recovered completely within 21 days.
Discussion and Conclusion: The majority of patients with severe AKI following Hypnale bites also have TMA. MAHA is the hallmark of TMA and process of red blood cell destruction within the microvasculature accompanied by thrombocytopenia due to platelet activation and consumption.
The presence of TMA is associated with a more prolonged course of AKI. In our patient, we have started plasma paresis early and it resulted in early recovery of both MAHA and AKI. Early initiation of plasma paresis would alter the course of the disease in patients with severe AKI and TMA following hump nosed pit viper bite envenomation.

Acute Kidney Injury (including CKRT)

P3-466 - Relation between capillary refill time and outcomes as acute kidney injury in post-cardiovascular surgery pediatric patients

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Background: Worldwide incidence of acute kidney injury (AKI) in children is 14%. In inpatient children, AKI can be up to 53%, and in post-cardiovascular surgery, up to 24%. The capillary refill time (CRT) and serum lactate are proposed have been proposed as predictive factors for AKI occurrence.
Objective: To evaluate the CRT and serum lactate levels as risk factors for AKI in children in post-cardiovascular surgery
Methods: An observational prospective study was conducted. Between October 2020 and March 2021, patients aged two years old or less who went to cardiovascular surgery were included. Logistic regression was performed to assess the association.
Results: Seventy-seven patients were included. The AKI incidence was 23.4% (50% KDIGO stage 1, 27.8% KDIGO stage 2 and 22.2% KDIGO stage 3), overall mortality was 10.4% and in AKI group was 22%. A CRT>4 seconds presurgical (OR: 6.93 CI 95% [1.97-24.35]; p=0.003) was associated with AKI occurrence. Regarding serum lactate, higher levels at ICU arrival (OR: 1.21 CI 95% [1.02-1.44]; p=0.03), 6-hours (OR: 1.25 CI 95% [1.04-1.5]; p=0.019) and 12-hours (OR: 1.26 CI 95% [1.04-1.52]; p=0.02) were associated with AKI.
Conclusion: CRT >4 seconds and higher serum lactate levels were associated with AKI occurrence in post-cardiovascular surgery pediatric patients.

Acute Kidney Injury (including CKRT)

P3-467 - Acute renal failure as a predictor factor for multiple organ dysfunction in preterm newborns

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Background: Multiple organ dysfunction (MOD) increases the risk of morbidity and mortality in newborns and its incidence is inversely proportional to weeks of gestational age (WGA). Preterms could have an increased risk of acute kidney injury (AKI) due to immature kidney function.
Aim: To estimate the association between AKI and MOD in newborns from a neonatal intensive care unit
Methods: Retrospective cohort study. Patients less than 37 weeks of WGA were included. Patients with NICU discharge or death within the first 24 hours of life were excluded. The population was divided according to MOD presence. Logistic regression was performed to assess associations.
Results: 273 patients admitted to the NICU who met the criteria were included. DOM incidence was 74.3%. AKI incidence was 12.5%, being 15.3 in the DOM group and 4.3 in the non-DOM group. For logistic regression, the weight and APGAR variables were excluded due to collinearity with WGA. After adjusting for WGA, AKI was associated with MOD (OR 3.83, 95% CI [1.07-13.69]; p=0.039).
Conclusions: AKI is associated with MOD. This study establishes an important precedent on morbidity generated by AKI in newborns. Monitoring renal could significantly impact patient clinical outcomes.

Acute Kidney Injury (including CKRT)

P3-470 - Risk factors and outcomes of severe acute kidney injury in children undergoing haematopoietic stem cell transplant

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Background: Acute kidney injury (AKI) is a well-recognised complication of haematopoietic stem cell transplant (HSCT). Previous studies have conflicting results regarding risk factors for AKI and have not assessed the association between baseline glomerular hyperfiltration (GH) and AKI in this population. We examined the relationship between AKI, transplant variables, and GH to further understanding of paediatric HSCT-associated AKI.
Methods: This was a retrospective review, across two tertiary paediatric hospitals. All patients undergoing allogeneic HSCT for haematological malignancy were included. AKI was defined and staged according to KDIGO criteria. GH was defined as glomerular filtration rate (GFR) ≥160mL/min/1.73m^2. Baseline and treatment related factors were included in univariate and multivariate analysis.
Results: 202 patients were included. Median age was 8.8 years (range 0.6-19 years). Within 100 days post-HSCT, AKI occurred in 85.6% of patients and 28.7% of all patients developed Stage 3 AKI, with 4.5% receiving kidney replacement therapy (KRT). Factors associated with development of Stage 3 AKI on multivariable analysis were early onset of AKI on or before day 10 (p=0.001), ≥10% increase in creatinine in the first 24 hours after AKI onset (p=0.001), use of ciclosporin (compared with tacrolimus) (p=0.02), and total body irradiation (p=0.01). When baseline GFR was included in multivariable analysis, higher GFR was associated with Stage 3 AKI (p=0.03). Estimated GFR at 1 year was significantly reduced in those with Stage 3 AKI compared to all others (-53.9 vs. -18.8mL/min/1.73m^2; p=0.0002). Mean five-year survival was significantly reduced in those who underwent KRT (74 days vs. 1289 days; p=<0.001).
Conclusion: Stage 3 AKI is prevalent among children undergoing HSCT and has significant consequences. New factors associated with severe AKI were identified, including early development of AKI and ciclosporin use. Higher baseline GFR may also be a risk factor for AKI and warrants further investigation.

Acute Kidney Injury (including CKRT)

P3-472 - Assessment of South Asian Pediatric Acute Kidney Injury Epidemiology and Risk Factors (ASPIRE): A Prospective study on 'Severe Pediatric AKI'

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Background& Objective: Pediatric acute kidney injury (AKI) is a global health concern, and the mortality associated with this is disproportionately higher in resource-limited settings when compared to high-resource settings. There is a pertinent need to understand the epidemiology of pediatric AKI; therefore, we aimed a prospective study (ASPIRE) to investigate the epidemiology and associated risk factors of 'severe AKI- which needs dialysis' in children among South Asian Nations.
Methods & Study Design: ASPIRE is a multi-center, prospective observational study was conducted in different hospitals from South Asian countries from January 2020-December 2021. All children and adolescents ≤18 years of age, who needed dialysis for AKI in any of the 21 collaborating centers were enrolled. Meticulous history and detailed data collection were performed until one of the following endpoints were observed: 1) Discharge with full recovery; 2) Death; 3) Discharge against medical advice. Data was analyzed in SPSS version 20.0.
Results: A total of 308 children with severe AKI were enrolled. The mean age was 6.17±4.65 years with males being 63%. Secondary AKI was more prevalent than primary AKI (62.7% vs 32.8%). Secondary AKI predominantly occurs due to infections (46.8%), dehydration (24.1%), and nephrotoxins-induced AKI (14.4%). Common causes of primary AKI were Glomerulonephritis (19.8%), hemolytic uremic syndrome (16.8%), lupus nephritis (15.8%), and obstructive uropathy (12.8%). Mean serum creatinine (mg/dl) at the time of diagnosis was 4.71±6.4 (mg/dl). Most of the patients presented with oliguria 53.2%, and only 27.6% presented with anuria. Shock, need for ventilation support, and coagulopathy significantly correlated with developing AKI. The foremost used renal replacement therapy was peritoneal dialysis (60.7%). The mortality rate was 32.1% among the study populations.
Conclusion: Common causes of AKI in children in southeast Asia are infections, dehydration, and nephrotoxins, which can be easily preventable. Mortality is high among these children suffering from severe AKI.

Acute Kidney Injury (including CKRT)

P3-473 - Acute Kidney Injury in Children with Dengue Fever: A Rising Concern in Bangladesh

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Background & Objective: Dengue has arisen as the most relevant viral infection represents a significant threat to public health. Acute kidney injury (AKI) is not uncommon and is a severe complication of dengue fever. There is a scarcity of data on pediatric AKI in dengue fever from Bangladesh. Hence this study was aimed to evaluate the incidence, characteristics, and clinical outcome of dengue fever with AKI.
Method: We retrospectively reviewed medical records of patients ≥14 years admitted with a diagnosis of dengue fever either by NS1 positive or antibody IgM positive or both IgM and IgG positive at Dr. M R Khan Children's hospital & Institute of Child Health, Dhaka from January 2019 to December 2021 with the approval of the ethical committee of the institute. Incomplete data were excluded. AKI was diagnosed according to KDIGO criteria. Detailed evaluations of clinical and laboratory data were performed and analyzed by SPSS version 20.0.
Result: Of the 712 total dengue patients, only 33 (4.6%) had acute kidney injury. The majority (54.5%) had stage-1 AKI, 30.4% had stage-2 AKI, and 15.1% had stage-3 AKI needed peritoneal dialysis. Mean HCT in AKI is higher than Non-AKI group 43.49 ± 3.47 Vs.37.98 ± 5.16, respectively, which is statistically significant (p-value <0.005). Mean serum creatinine (µmol/L, mean ± SD) was 187.17 ± 121.35 in AKI group & 84.25 ± 16.99 in Non AKI group which is statistically significant (p-Value <0.001). The duration of hospital stay was more in stage-3 AKI than stage 1 & stage 2. Three patients died in stage-3 AKI group mortality is 9%.
Conclusion: AKI in children with dengue is not uncommon. Dengue associated with AKI had significant mortality and morbidity.

Acute Kidney Injury (including CKRT)

P3-474 - Acute kidney injury(AKI) in multisystem inflammatory syndrome (MIS-C), a single center experiences in Bangladesh

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Background: Multisystem Inflammatory Syndrome in children (MIS-C) is a newly identified entity during covid pandemic. Although Acute Kidney Injury has been reported in patients with covid -19 infection, there is no such data about MIS-C patients.
Methods: This is a retrospective study conducted during the period of May 2020 to April 2021, in Pediatric department of Evercare Hospital Dhaka, Bangladesh. Patients who met CDC criteria of MIS-C were included in the study group and they are evaluated for presence of AKI or not, according to KDIGO guideline
Results: Total forty (40) patients were included in the study. Mean age was (64.22 ±50.06) months. Range was (4-177) months. Male was 24(60%), Female was 16 (40%). Duration of mean Hospital stay was (7.58±3.86) days. All of them got steroid and 23 (57.5%) of them got IVIG. Among the 40 patients, 13 (32.5%) patients were found to have AKI. There was no mortality. Among the AKI patients, all were in, KDIGO stage one, except 3 patients. No patient needs dialysis. Twelve percent patients needs PICU admission.
Conclusion: Our study suggests that children with MIS-C, mostly experiences mild AKI, and all of them improved promptly with only supportive management.

Acute Kidney Injury (including CKRT)

P3-476 - Novel Biomarkers in Childhood Acute Kidney Injury: A Meta-analysis of Diagnostic Test Accuracy

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Background: Early accurate recognition of acute kidney injury in children may improve morbidity and mortality. Traditional diagnosis of AKI by serum creatinine and urine output has inherent limitations and may delay diagnosis. Novel non-invasive biomarkers ushered a new era that may allow early recognition of AKI.
Methods: This meta-analysis aimed to quantitatively synthesize the diagnostic performance of the novel biomarkers in predicting AKI. We searched PubMed, EMBASE, and Web of Sciences for studies published till January 2022. Search terms included acute kidney injury, pediatrics, adolescent, and biomarker. Two reviewers independently assessed the studies for eligibility. Cohort and cross-sectional studies evaluating the diagnostic performance of various biomarkers in predicting AKI. The QUADAS-2 tool for quality assessment. The hierarchical summary receiver operating characteristic (HSROC) model was used to synthesize the summary estimates of diagnostic parameters. Diagnostic accuracy was reported using summary sensitivity, specificity, and area under the curve (AUC) with 95% CI.
Results: Overall, thirty-five studies were included in this meta-analysis. Urinary NGAL showed summary sensitivity, specificity, and AUC of 0.75 (95% CI, 0.61–0.86), 0.84 (0.73–0.91), and 0.87 (0.84–0.89) respectively for the prediction of AKI in children who underwent cardiac surgery. In the setting of the intensive care unit (ICU) AUC was 0.81 (0.77-0.84) for the prediction of AKI. Similarly, the AUC of serum NGAL for ICU and cardiac surgery patients was 0.83 (0.80-0.86) and 0.92 (0.90-0.94), respectively. We observed a pooled AUC of 0.83 (0.79-0.86) for serum cystatin C in an ICU setting in the prediction of AKI. The AUC of IL-18 for predicting AKI was 0.73 (0.69-0.77).
Conclusion: Pooled evidence suggests that NGAL and serum cystatin C have good predicting ability and may have potential role in early recognition of patients at higher risk of AKI in routine clinical practice.

Acute Kidney Injury (including CKRT)

P3-477 - Cucurbitacin B reduce lipopolysaccharide-induced acute kidney injury by down-regulating monocyte chemoattractant protein 1 and high mobility group box 1 protein

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Objective: To explore whether Cucurbitacin B(CuB) has protective effect on septic acute kidney injury and its mechanism.
Methods: The 25 mice of C57BL/6 were equally divided into control group, LPS group, LPS + CuB 0.2 mg/kg group, LPS + CuB 1 mg/kg group and LPS + CuB 5 mg/kg group. In CuB pretreatment groups, mice were fed with CuB at different doses for 5 days, Then, mice were injected 5mg/kg LPS intraperitoneally, after 20 hours mice were killed. Serum urea nitrogen and creatinine were detected. Kidney injury molecule 1(KIM-1) and Neutrophil gelatinaseassociated lipocalin(NGAL), MCP-1 and HMGB1 expression in kidney tissue were detected by qPCR. Renal pathological were observed by HE staining and PAS staining. Renal MCP-1 expression were detected by immunohistochemical. Serum cytokine interleukin-10 was detected by Elisa.
Results: 1. In the LPS group, the serum urea nitrogen increased, (P <0.05). Compared with the control group, mRNA expression of NGAL and KIM-1 in renal were elevated, (P <0.05).
2.In 0.2 mg/kg and 1 mg/kg pretreatment groups, the renal tubular injury score was lower than that in the LPS group. there was no difference between LPS + CuB 5 mg/kg group and LPS group.
3. Compared with LPS group, the urea nitrogen of cucurbitacin B pretreatment group was decreased (P<0.05), the mRNA expression of KIM-1, NGAL, HMGB1 and MCP-1 were reduced (P<0.05).
4. The renal protein expression of MCP-1 renal of LPS group was upregulated (P<0.05).
5. Compared with the LPS group, serum cytokine IL-10 levels increased (P<0.05).
Conclusions:
1. Cucurbitacin B pretreatment can reduce acute kidney injury induced by lipopolysaccharide.
2. Cucurbitacin B reduces acute kidney injury via down-regulating MCP-1, HMGB1in renal and up-regulating the level of serum IL-10.

Acute Kidney Injury (including CKRT)

P3-478 - Chronic after acute tubulo-interstitial nephritis (TIN) in a paediatric inflammatory bowel disease patient.

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Introduction: Inflammatory bowel disease is a chronic immuun-mediated multisystem disorder. Extra-intestinal manifestations can cause significant morbidity and the disease itself has been associated with interstitial nephritis (TIN). In order to treat IBD, 5-aminosalicylates are commonly prescribed. They are however known for having a wide range of adverse effects, inclusive TIN
Case description: We present a case of a 17-year-old male known with an undifferentiated type of IBD who is being treated with mesalazine. At the age of 13 years old, he was referred because of a rise in serum creatinine. Kidney biopsy showed acute tubulo-interstitial nephritis, with a lot of inflammation diagnosed as mesalazine-related. Mesalazine was stopped and corticosteroids were initiated, upon which full remission of TIN was accomplished. Three years later, a rise in serum creatinine as well as in tubular proteinuria was noticed. A second kidney biopsy showed signs of a chronic tubulo-interstitial nephritis with a lot of fibrosis. It remains unclear whether this chronic nephritis is due to the mesalazine exposure or if it is rather linked to the inflammatory bowel disease itself.
Conclusion: The initial acute tubulo-interstitial nephritis episode was considered as an adverse effect of mesalazine, with full remission after withdrawal of the drug. However the relapse in absence of mesalazine demonstrates the evolution into chronic form of the drug induced tubulo-interstitial nephritis secondary or an extra-intestinal manifestation of the inflammatory bowel disease

Acute Kidney Injury (including CKRT)

P3-479 - Retrospective analyses of epidemiology and risk factors of hospital-acquired acute kidney injury at a tertiary children's hospital in Japan

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Background: Several reports have suggested that hospital-acquired acute kidney injury (HA-AKI) in children is common as adults. However, some of them are focused exclusively on critically ill patients, and others conducted with limited background diseases. Risk factors of HA-AKI in generally hospitalized children have not been fully elucidated.
Methods: We retrospectively analyzed incidence and risk factors of HA-AKI in a cohort of 802 children aged 2 to 18 years who had admitted at our single institution between 2018 and 2019. AKI was defined as a serum creatinine change by a 50 % increase from the baseline. We firstly identified any patients of AKI with digital medical records and categorized them as HA-AKI or not. Patients were identified as HA-AKI if AKI was not apparent upon admission nor within 24 hours of admission, but developed during hospitalization. We registered patients' place of admission (intensive or general ward), diseases that required hospitalization, details of treatment, and renal function prior to HA-AKI.
Results: Seventy patients with AKI were identified. Forty patients, 5.0 % of total for analysis, developed HA-AKI, of which 16 had in general wards. Only 15 patients confirmed to have timely and appropriately diagnosed as HA-AKI. The major cause of hospitalization was congenital heart diseases, contributing 45 % of cases, and 6 had renal dysfunction prior to HA-AKI. All patients were exposed to nephrotoxic drugs and 17 had surgery prior to HA-AKI. Renal dysfunction prior to HA-AKI and administration of furosemide and vancomycin were associated with a higher risk of HA-AKI with multivariate analysis.
Conclusions: The present study revealed that HA-AKI in children is substantially underdiagnosed. Further commitment by pediatric nephrologists is warranted to improve awareness of HA-AKI. In preventing HA-AKI, more attention should be paid to children treated with furosemide or vancomycin, as well as those with chronic kidney disease.

Paediatric nephrology in under-resourced areas

P3-480 - Posterior urethal valves in a tertiary hospital in South Western Nigeria: preliminary analysis of a five-year review

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Introduction: Posterior urethral valve (PUV) is the most severe form of congenital obstructive uropathy. Detection and management of PUV

may be challenging in many parts of sub-Saharan Africa. To provide recent data on PUV in Nigeria, we reviewed the cases that were admitted into our hospital.
Methods: Information was obtained from the paediatric nephrology and paediatric surgery data base of children admitted to the University College Hospital Ibadan with a diagnosis of PUV over a 5 year period-March 2016- February 2021.
Results: 47 cases were reviewed. Their ages ranged from 2 days to 12 years (median age 1.4 years). Antenatal detection of anomalies of the urinary tract was made in 2 patients.
18 (38.3%) presented during the first year of life and of this number, 3 (6.4%) presented in the neonatal period. The commonest complaints at presentation were abdominal distension (51.1%), urinary stream abnormalities(31.9%) and straining to pass urine in 36.2%.
Review of abdominal ultrasound in 43 showed that bilateral hydronephrosis was noted in 72.3%, while bilateral hydroureters was noted in 51.1%. Micturating Cysthourethrogram results available for review in 19 showed bilateral VUR in 3 and unilateral VUR in 4.
Six patients had valve ablation before presentation- 4 in outside facilities, while 2 patients had valve ablation done in our centre before the study period. A total of 25 (53.2%) of patients underwent valve ablation (Mohan's or endoscopic valve ablation).
6 patients were in ESRD, 4 patients underwent acute intermittent haemodialysis while 1 patient underwent acute peritoneal dialysis. In-hospital mortality occurred in 8 (17%) patients
Conclusion: PUV is relatively common in our setting. Increased antenatal detection, early presentation and interventions are required to further improve outcomes.

Paediatric nephrology in under-resourced areas

P3-481 - Assessment of health-related quality of life of children with chronic kidney disease on follow up at pediatric renal clinic, tikur anbesa specialized hospital, addis ababa, ethiopia

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Background: Children with chronic kidney disease face lifelong increases in morbidity, mortality, and decreased quality of life. As most of other chronic illnesses, CKD has hard impact on ill children's and care givers life style, peer relationship, pain interference and social functioning moreover CKD has impact on intellectual functions and behavioral characteristics including anxiety and depression.
Objective: To assess health related quality of life of children with CKD as well as their caregivers‟ perception on their Childs performance and to determine the factors that adversely affect it.
Methods and material: A cross-sectional analytical study conducted using a pre coded, pretested structured questionnaire including PedsQoLTM 4.0 scale score generic core and family impact module. Data obtained for demographic and clinical parameters of children and for each domain of generic core and family impact module and data was analyzed using IBM SPSS® version 26.
Results: 105 children with CKD aged 2-18 years, 61(58.1%) males and 44(41.9%) females were included in this study. Among the child self reported domains of generic core scale, child‟s „school performance‟ was most affected with mean of 74.91 (SD±22.29) followed with child „physical performance‟ 77.6±26.41. In the family impact module domains with mean also, the most affected being „school performance‟ with 75 (SD±19.89) followed with „physical functioning‟ with 78.13 (SD±24.96).
Recommendation: School performance‟ and „physical functioning‟ were the most affected domains in child generic scale and family impact modules. Optimal care requires attention not only to medical management, but also to an assessment of health related Quality of Life factors, that may help promote pediatric CKD patient‟s health like Implementation of a standardized tool and Multidisciplinary approach in addressing HRQoL in all CKD patients on follow up.

Paediatric nephrology in under-resourced areas

P3-482 - Whole exome sequencing in children with renal tubular disorders: Initial report from Indian Tubulopathy registry

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Introduction: renal tubular disorders are a group of rare diseases characterized by phenotypic and genotypic heterogeneity. Affected children may have multisystem involvement and life-threatening complications with adverse impact on quality of life of the patients and family members. The low prevalence, phenotyping variability and paucity of clinical and biological data further restrain our knowledge of renal tubular disorders and their impact on health. The genotype-phenotype correlation of monogenic renal tubular disorders is inadequately studied across populations due to low prevalence and inadequate resources.
Objectives: The objectives of this ongoing registry and biorepository are (a) to identify pathogenic/likely pathogenic variations in a set of genes associated with renal tubular disorders using whole exome sequencing and (b) to track medium term clinical outcomes that are associated with the phenotype and genotype.
Results: A total of 100 children with tubular disorders were enrolled in the registry over a 1-year period from nine centers across India. Genetic studies were available from 40 children in this ongoing national registry and biorepository. The men age of the patients was 9.26 (±3.4) years. Phenotyping diagnosis of dRTA (35); distal RTA with amelogenesis imperfecta (4); Bartter syndrome (8) Gitelman syndrome (2), renal Fanconi syndrome (6); proximal RTA (7). A total of 44 variants were detected; of these, 31 were pathogenic or likely pathogenic. Of 27 patients with dRTA in whom NGS report is available, the diagnosis 20 patients were confirmed through genetic testing (diagnostic yield: 74. %); the most common mutation was *ATPV1B1* (n=8); WDR72(5); *SLC4A1*(n=4); and *ATP6V0A4*(n=3). Diagnosis was revised in 3 patients (tyrosinemia; cystinosis; Fanconi reno-tubular syndrome).

Conclusion: NGS is helpful diagnostic tool for diagnosis and management of patients with tubular disorders.
Funding: The project is funded by extramural grant of Indian council of Medical Research (ICMR) task force on rare disease (33/12/2019/TF/Rare/BMS

Paediatric nephrology in under-resourced areas

P3-483 - Current State of Pediatric Kidney Replacement Therapy (KRT) Around the Globe. Findings from the IPNA KRT Registry.

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Background: The IPNA KRT Registry collects information on pediatric chronic kidney replacement therapy (cKRT) worldwide.
Methods: Data including primary renal disease (PRD), cKRT start date, initial modality and modality changes are either transferred from existing national registries or entered directly via an online platform (www.ipna-registry.org). Patients are followed prospectively from the start of cKRT until transfer to an adult center, death, or loss of follow up.
Results: Currently, the Registry oversees 77 countries representing 60% of the global childhood population. Another 45 countries encompassing 13% of the world's childhood population do not offer any pediatric cKRT. We analyzed data of 14.800 children commencing cKRT between 2000-2020. The commonest PRD leading to cKRT worldwide was CAKUT (38%), while glomerular diseases were more common in South-East and South Asia (43% and 36%). The prevalence of CKD of unknown origin (14%) was inversely associated with GDP ($p< 0.01$). HD was the first-choice cKRT modality worldwide (42%), followed by PD (38%) and pre-emptive Tx (18%). PD was the most popular initial modality in Latin America (56%) and Turkey (49%). The median age at cKRT start was 10.7 (IQR 5.8-14.3) years. The fraction of infants <2 years starting cKRT ranged from more than 25% in Western Europe to none in some African and Latin American countries. Infection (22%), cardiac causes (9%) and "sudden death/unknown" (37%) were the most common cause of death. The risk of death was significantly increased on dialysis vs. post-transplant state (HR 2.5, CI 1.95-3.40), low GDP (HR 0.72, CI 0.68-0.75) young age (HR 0.96, CI 0.94-0.97); (all $p<0.0001$) and female sex (HR 1.2, CI 1.07-1.38; $p<0.01$).
Conclusion: Access, choices and outcomes of pediatric cKRT vary widely worldwide. The IPNA Registry allows to compare up-to-date country specific information to support efforts to optimize access and outcomes of pediatric cKRT on the global level.

Paediatric nephrology in under-resourced areas

P3-484 - Pattern of Paediatric Urologic Disorders presenting to the Paediatric Nephrology Unit of Rivers State University Teaching Hospital, South South Nigeria: A 5 - year Retrospective Review

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Background: Paediatric urologic diseases are predominantly congenital in origin and are a risk for progression to end stage kidney disease. This study aims to describe the pattern of childhood urologic diseases that present to the paediatric nephrology clinic at the Rivers State University Teaching Hospital (RSUTH), Port Harcourt, Rivers state, Nigeria.
Methods: A review of case records of all children aged less than 18 years seen at the paediatric nephrology outpatient clinic over a period of 5 years (2015-2019) were studied.
Results: A total of 10,372 children were seen during the study period with 40 of them had urologic disorders, giving a prevalence of 0.03% (3.8 cases per 1000 children). There were 30 (75%) males and 10 (25%) females, with a male to female ratio of 3:1. The ages ranged between 2 weeks and 16 years. The commonest urologic disorders were posterior urethral valves 16 (40%) ectopic kidneys 7 (17.5%) followed by urethral strictures 5 (12.5%), urethral prolapse and urethrocoele 3 (7.5%) each, ureteropelvic junction obstruction with hydronephrosis, hypospadias and renal tumours were the least occurring, accounting for 2 (5%) each.
Conclusion: The commonest urologic disorders seen in the paediatric nephrology clinic of RSUTH is the posterior urethral valve which is amenable to surgery, if detected early. There is need to create awareness of this condition to aid early detection and to retard progression to end stage kidney disease in this setting.

Paediatric nephrology in under-resourced areas

P3-485 - Paediatric nephrology in under-resourced areas

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A little more than half of the worldwide people, including more than 60% of children between the ages of 0 and 14 years, live in middle-class income nations. In many nations, pediatric nephrology (PN) is not a top priority when it comes to allocating scarce healthcare resources[1]. This article examines the progress that has been accomplished as well as the limits that still exist in delivering appropriate PN support for children in certain under-resourced communities (URA). For data, the ISN, as well as IPNA headquarters, were visited, and two survey questionnaires polls of IPNA participants were conducted to gather information. Members of the IPNA's regional chapters were approached for further in-depth information. There is a paucity of available research within URA; when data is accessible, it is often claimed that the incidence of PN illnesses, their care, and their results vary from those

seen in high-income countries. Human resource limitations, as well as inadequacies in fluoroscopy, fluorescence, scanning electron, as well as genetic research, were discovered. A number of medications, as well as maintenance renal replacement treatment, is beyond reach for the vast majority of patients[2]. Despite these difficulties, regional initiatives, with the assistance of international organizations, have resulted in major improvements in PN services and infrastructure in a number of URA. URA continues to face significant issues in the areas of equitable distribution and cost of PN services. A sustained effort should be made to acquire regional statistics, advocate for local government and non-governmental organizations, and collaborate with international support organizations. An initial emphasis will be placed on diseases that are avoidable and reversible with the goal of optimizing and achieving worldwide equity in PN training, investigations, as well as treatments.
Keywords: Kidney replacement therapy; Low-income country; Low-middle–income country; Paediatric nephrology; Under-resourced.

References

Paediatric nephrology in under-resourced areas

P3-486 - Pediatric Nephrology Volunteerism in Under-Resourced Settings- A collaboration between IPNA, ASPN, and Health Volunteers Overseas

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Introduction: There is widespread need for high-quality training in pediatric subspecialties in under-resourced countries. Many pediatric nephrologists are interested in providing nephrology-focused education in these settings, however, opportunities for in-person volunteering have been limited because of the SARS-Cov-2 pandemic. Internet-based "virtual" volunteerism has become a time and cost-efficient method for providing high-quality nephrology education in under-resourced settings.
Materials and Methods: In 2019, the International Pediatric Nephrology Association (IPNA), the American Society of Pediatric Nephrology (ASPN), and Health Volunteers Overseas (HVO) signed an agreement to develop opportunities for nephrologists to volunteer in under-resourced countries. We used an online platform developed by HVO to organize, schedule, reposit, and host virtual seminars for an introductory nephrology curriculum developed in collaboration with pediatricians at Angkor Hospital for Children (AHC) in Siem Reap, Cambodia.
Results: With the support of IPNA and ASPN, HVO has been able to recruit, vet, orient, and support lectures from 5 pediatric nephrologists, with over 18 expressing interest in participation. To date, 13 virtual sessions have occurred with students and faculty from AHC in Siem Reap, Cambodia. Topics have ranged from fluid and electrolyte disorders to glomerular diseases. Feedback from volunteers and students has been uniformly positive. Surveyed students commented that the seminars were especially valuable teaching tools because of the utility of shared experiences and the clinical relevance of kidney-focused topics. As of February 2022, the project is being expanded to two additional sites in Kampot, Cambodia, and Kampala, Uganda.
Conclusions: The global pandemic has forced a shift from in-person to online volunteering for health care providers. The pediatric nephrology community has adapted to these circumstances by partnering with an experienced non-governmental organization to provide high quality kidney-focused lectures in under-resourced settings.

Paediatric nephrology in under-resourced areas

P3-488 - Sharing knowledge and experience to make a difference: Launching our Uganda – Baylor College of Medicine ISN Sister Renal Center Program initiative amidst the COVID-19 pandemic

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Background: In January 2020, we were awarded a level C grant to support educational activities for a new collaboration between the Paediatrics Kidney Unit at the Mulago National Referral Hospital in Uganda and Baylor College of Medicine and Texas Children's Hospital in the United States. Our goal was to expand paediatric knowledge beyond the referral hospital by conducting in-person educational meetings across various health facilities.
Approach: With the COVID-19 pandemic, we reevaluated our approach, and submitted a request for reallocation of funds to facilitate virtual educational activities. Posters for each session were developed and distributed via WhatsApp messaging system and through emails to various health care provider groups. In April 2021, we launched bi-monthly paediatric nephrology virtual educational series and case discussions led by participants. We also used the funds to host a radio program to increase awareness in childhood kidney diseases.
Achievements: Participants included physicians, nurses, pediatric postgraduate students, medical students, and other allied health professionals in pediatric care. Bi-weekly virtual synchronous lectures series were conducted via Zoom. Topics covered included nephrotic syndrome, AKI, congenital anomalies of the kidney and urinary tract, CKD, AKI in malaria, nursing management of NS, kidney transplantation, and considerations when initiating dialysis. Participants were invited to present relevant clinical cases which were discussed by content experts. The funds were also used to facilitate participants' access to internet services to attend the virtual talks and host radio and TV talk shows to raise awareness of childhood kidney disease.
Conclusion: The focus for the first 2 years has been development of multidisciplinary educational exchanges between the emerging and supporting centers. This new collaboration has allowed us to share knowledge with more people than we anticipated. Following this successful level C project implementation, we are excited to apply for an upgrade to level B in 2022.

Paediatric nephrology in under-resourced areas

P3-489 - Experiences in Paediatric Nephrology services in a resource limited setting - tertiary care Centre in North Karnataka, India

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Background: The burden of kidney diseases in paediatric population is growing globally, particularly in low- and lower-middle income

countries (LLMICs) where access to treatment is poor and facilities available are limited. This article explores the limitations faced by treating physician and difficulties for parents of children who are suffering from various kidney diseases like acute kidney injury (AKI), chronic kidney disease (CKD), haemolytic uremic syndrome (HUS) in resource limited settings like India.
Settings and Design: It is a retrospective study conducted during the period of January 2021 to January 2022 among paediatric patients attending outpatient department and admitted in Paediatric nephrology department of Dr Prabhakar Kore Hospital and MRC, Belagavi, Karnataka, India. Data collected from outpatient and admission records.
Results: Majority of patients with AKI are managed acutely with haemodialysis or peritoneal dialysis due to the unavailability of continuous renal replacement therapy (CRRT). Complement mediated diseases like HUS are being managed with limited options due to unavailability of Eculizumab resulting in prolonged hospital stay, morbidity and mortality. Majority of patients with CKD are managed conservatively without proceeding to continuous ambulatory peritoneal dialysis (CAPD) or chronic haemodialysis due to unavailability of the required resources . Also patients do not undergo renal transplantation as a cure because of financial constraints and the burden on a single earning member.
Conclusion: Acute kidney injury being completely reversible with good outcome and least sequalae, focus should be on improving the availability of resources to treat AKI with the help of various government and non government organisations (NGO). Better Government schemes to improve awareness and accessibility to renal replacement therapy including kidney transplantation should be the immediate goal to help children in resource limited settings like India.
Keywords: resource limited setting, AKI, HUS, CKD

Paediatric nephrology in under-resourced areas

P3-490 - Utility of serum adiponectin as novel biomarker of steroid resistance nephrotic syndrome

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Our main objective was to investigate the role of serum adiponectin as a biomarker of steroid resistance nephrotic syndrome. Nephrotic syndrome is primarily a glomerular disease in which a small proportion (~20%) of children present with or subsequently develop steroid resistance. Although renal biopsy remain an ideal diagnostic step to identify steroid resistance to date, few studies have reported that serum and urinary biomarkers are now being utilized as a discriminatory tool in distinguishing steroid-sensitive from steroid resistance nephrotic syndrome. It was recently reported that adiponectin is one of the candidate biomarkers with the potential to identify mechanistic molecular pathways and targets of steroid resistance.
We conducted a prospective observational study and enrolled a total of 60 children with nephrotic syndrome, of which 17 were SRNS cases (12 in relapse and 5 in partial remission),23 were SSNS cases and 20 were age and gender-matched controls. We measured their serum adiponectin levels at the time of enrollment and also at remission for SSNS cases only. A comparison of serum adiponectin levels was done between SRNS cases with SSNS in relapse and remissions and also with controls. The mean adiponectin level in SRNS was 9.12 +/- 2.4 mcg/ml was significantly higher than controls (2.18+/- 1.62 mcg/ml), SSNS during relapse (8.65 +/- 3.22 mcg/ml) and during remission (2.96+1.1 mcg/ml). The adiponectin levels in SRNS cases were increased both in relapse (9.22 +/- 1.93mcg/ml) and partial remission (7.22+/- 2.75mcg/ml) which was significantly higher than adiponectin in SSNS during relapse ($p<0.001$) and controls ($p<0.001$).
Elevated serum adiponectin levels in SRNS cases and failure to decline may point toward the possibility of the discriminatory role of this biomarker between steroid resistance and steroid sensitivity. Biomarkers are useful tools for diagnosis and prognostication in childhood idiopathic nephrotic syndrome, as well as for differentiating SRNS from SSNS.

Paediatric nephrology in under-resourced areas

P3-492 - From Tubular Acidosis to Metabolic Alkalosis: Is it possible?

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Introduction: Tubulopathies are a heterogeneous group of entities with alterations in tubular function. Bartter syndrome is an inherited tubulopathy. It is a rare disease with two to six genotypes. Characterized by metabolic alkalosis, genotype 2 initially presents with metabolic acidosis. Its rare presentation and infrequency of this tubulopathy in our environment, represents a diagnostic challenge. Objective: To describe the clinical course of a patient with Bartter's Syndrome with a mutation in the KCN1J gene. Methods / results Case report and literature review. A 9-year-old female patient, with consanguineous parents, premature, polyhydramnios at debut, presents renal tubular acidosis and acute renal failure. Reported recurrent episodes of urinary tract infection, growth retardation, nephromegaly and hypokalemia, requiring multiple hospitalizations for recurrent abdominal pain and dehydration. The patient is treated with sodium bicarbonate with a clinical picture change to a metabolic alkalosis. Bartter's syndrome is suspected. Subsequent examinations show osteopenia, nephrocalcinosis, hyperreninemia, and elevated aldosterone. Due to the use of prostaglandin inhibitor, diuretic and vitamins a significant improvement is manifested. It is confirmed by genetic study that it is a carrier of a homozygous pathogenic variant in the KCNJ1 gene, corresponding to type 2 Barter's syndrome with autosomal recessive inheritance. This is the first time that we describe this kind variant in our country. Conclusion: This case illustrates the variation in the clinical presentation of Bartter Syndrome, with a debut of tubular acidosis with subsequent metabolic alkalosis, consistent with this genetic variant (Type II). Identifying atypical tubulopathies is a great challenge. They require specific genetic diagnosis methods and multidisciplinary teams for early diagnosis to prevent future complications.

Paediatric nephrology in under-resourced areas

P3-493 - Higher rates of complicated urinary tract infection (UTI) among Aboriginal Children: a report from the Top End Health Service of the Northern Territory of Australia.

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Aim: To describe the presentation, bacteriology and antibiotic susceptibility of pediatric UTI in the Top End Health Service (TEHS) of the Northern Territory (NT).

Background: UTI hospitalization rates increase with remoteness and socioeconomic disadvantage. The NT has the highest proportion of people living in remote areas in Australia, the highest proportion of Aboriginal residents, and one of the highest burdens of chronic kidney disease in the world. Aboriginal children suffer higher burden of infectious disease, antibiotic prescriptions, and mortality compared to non-Aboriginal Australian children. To our knowledge, there is no published data describing the epidemiology of pediatric UTI in the NT.
Methods: A retrospective audit of culture-proven UTIs in symptomatic children ≤16 years presenting to TEHS between 2015-2017.
Results: There were 546 cases of UTI. The median age of presentation was 2.2 years, and 147 (39.8%) children were Aboriginal. Males were more likely to have pre-existing kidney condition (23.1% vs. 13.3%, $p < 0.01$). *Escherichia coli* accounted for 72.9% (n=398) of UTI. *E.coli* resistance to first-line oral agents were ampicillin 61.1%, cotrimoxazole 32.7%, and cephalexin 13.8%. Aboriginal children had higher rates of hospital admission (58.5% vs. 40.1%, $p<0.001$), acute kidney injury (7.5% vs. 3.9%, $p = 0.06$), bacteremia (10.3% vs. 3.3%, $p = 0.037$), and atypical imaging (26.1% vs. 13.0%, p=0.02), despite being older (median age 3.3 years vs. 2.0 years, $p = 0.02$), and having less pre-existing kidney disease (12.3% vs. 19.2%, $p = 0.03$).
Conclusions: *E.coli* is the most common cause of UTI in NT children, with higher-than-expected resistance to first-line oral antibiotics. Aboriginal children had higher rates of complicated UTI, highlighting the need for vigilance when assessing an Aboriginal child with fever. Prompt diagnosis and accurate treatment of UTI in Aboriginal children is important to optimize long-term kidney health, given the high burden of CKD in this population.

Paediatric nephrology in under-resourced areas

P3-494 - Knowledge, Attitude, and Practices regarding renal health among caregivers of children with renal diseases coming in Pediatric Nephrology Clinic.

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Introduction: Health depends on the knowledge, attitude and practices of the caregivers towards illness. It becomes important that studies be carried out to identify the specific gaps in knowledge, the fallacies in attitude and practices and correct them.
AIMS and Objectives: To assess the knowledge, attitude and practices for renal health among caregivers of children with kidney diseases.
Methodology: Cross sectional study in Rajasthan (India) over 2 months, where parents/caregivers of 88 patients with renal disorders were interviewed using a 4 part questionnaire with 25 items to assess the knowledge attitude and practices.
Results and Observations: 70% consulted for a male child, 47% from rural areas.
Knowledge: 64.7% of enrolled caregivers scored more than 50% . 11.36% caregivers did not know any function of kidney. 56.8% patients could not tell even a single cause of kidney failure. Only 10 caregivers (11.8%) could tell about the normal BP.
Attitude; 67% caregivers like the idea of learning more about their child's renal disease. 54.5% caregivers felt that kidney diseases are majorly prevalent in this region. Most of the parents (73.8%) thought they were highly stressed.
Most of our caregivers (40/88) considered that they had little knowledge and it was positively related to the total knowledge score. 60.22% cannot afford the cost of treatment. 20% caregivers believe that the health of their child will hamper their reputation in the society. Only 54.5% made a record of their child's disease. 17% caregivers avoid high salt diet .Most (92%) did not know about the harmful medications
Conclusion: Gaps like poor literacy and poor access to resources for information about their child's illness were identified. A large number of caregivers wanted to learn more about their child's renal disease (60%). Making a peer group of caregivers with similar disorders will enhance knowledge shraring and improve their attitude about their child's illness.

Paediatric nephrology in under-resourced areas

P3-495 - Assessment of the impact of risk variables on the growth of children and adolescents with chronic kidney disease stages 3 and 4: results from the SPCKDKID cohort

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Introduction: In children with chronic kidney disease (CKD), growth retardation is associated with higher morbidity and mortality.
Objective: to characterize the growth of children with stages 3 and 4 CKD in relation to the frequency of short stature and its evolution over the observation period and to identify impact factors associated with growth deficit.
Methods: This is the analysis of data collected by the prospective and multicentric cohort, involving 209 Brazilian pediatric patients followed by CKD (stages 3 and 4), in seven medical centers in the state of São Paulo (SP- CKDKID). A descriptive analysis of factors related to growth was carried out, observing the evolution of growth throughout the visits, during 2 years of follow-up. To assess growth over the observation period, the delta Z Height score was calculated, considering the first and last visit. In the evaluation of the variables, the median and the interquartile range (IQR) were used to describe the quantitative variables and frequency tables for the qualitative variables. The effect of each possible risk factor was evaluated by the chi-square test**.**
Results and conclusion: after follow-up period, there was a 10% increase in the prevalence of short stature, and it was observed that the variables of impact to height growth were: age group <3 years ($p=0.019$) - as a positive factor for growth - and serum bicarbonate < 20 mmol/L ($p=0.029$) - as a negative factor for growth. The results of this cohort may reflect the socioeconomic conditions of the population studied and evidence the importance of early access to quality health care, in line with the results of other cohorts that studied growth retardation in CKD, present in the literature.

Key words: chronic kidney disease; CKD stages 3 and 4; Growth; Growth deficit; Short stature.

Paediatric nephrology in under-resourced areas

P3-496 - A comparison of the CKiDU25 and Modified Schwartz equations in screening for reduced glomerular filtration in school children.

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Background: The new improved Chronic Kidney Diseased in Children (CKiD) equation for estimation of glomerular filtration rate (eGFR) in individuals under the age of 25y (CKiDU25) is an improvement compared to the more popular bedside Modified Schwartz equation. In this study, we compared the 2 equations in a screening exercise for reduced GFR in school children in Kano, Nigeria.
Methods: We screened 273 school children for body mass index (BMI), albumin creatinine ratio (ACR) using spot urine samples and serum creatinine from blood samples. We used both the Modified Schwartz and CKiDU25 equations to calculate the eGFR of the students
Results: Median age was 12.7y (11.1-13.8), 141 males and 132 females. The eGFR from the CKiDU25 equation had a significantly lower mean compared to mean eGFR from the Modified Schwartz equation (101 ± 19 ml/min/1.73m^2 < 108 ± 20 ml/min/1.73m^2, $p<0.001$). Age group sub-analysis showed a similar finding, being more distinct in children <10years. More children with reduced eGFR (<90 ml/min/1.73m^2) were noted when the CKiDU25 equation was used. The eGFR calculated from the CKiDU25 equation showed small correlation with both BMI (r=0.15, p=0.016) and ACR (r= -0.133, p=0.029), this was not seen in eGFR calculated from the Modified Schwartz equation
Conclusion: Estimated GFR using the CKiDU25 equation was able to pick up more children with mild reduction in eGFR compared to the Modified Schwartz equation. The CKiDU25 eGFR showed small correlation with BMI and ACR, not seen with the eGFR from the Modified Schwartz equation. The above findings suggest that the CKiDU25 equation is more sensitive in picking up early decline in GFR compared to the Modified Schwartz equation. However, a more robust study will need to be conducted to confirm this assertion.

Paediatric nephrology in under-resourced areas
P3-497 - Healthcare Scientists and Primary Care – A Systematic Review

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Introduction: The UK is seeing a continuing and important shift in the burden of disease, from mortality to morbidity. Much of the health burden is preventable. Much of monitoring in chronic kidney disease (CKD) patients occurs in mild/moderate disease by General Practitioners (GPs), with only the final stages of disease managed in secondary care. Patients with Type 2 Diabetes (T2DM) and CKD, are now being promoted to self-care more and take ownership of health. In turn, this also means that access to education relating to disease management in the National Health Service (NHS) faces ongoing challenges.
Aims: Conducting a systematic review over an 18-year duration, this work will seek to describe what the educational and support pathway for CKD could look like with Healthcare Scientist involvement to provide supplementary education surrounding this Long-Term Condition (LTC). This work will also seek to understand if CKD patients could attain more informed education for disease management and laboratory tests and investigations. This work will finally outline if now it is the right time for Healthcare Scientists to be involved in Primary Care to best practice.
Design: A systematic review was conducted over an 18-year period. A Critical Appraisal Skills Programme (CASP) was used to appraise papers.
Results: From the 1,481 papers identified via several databases. 1,493 records removed, 30 papers were further scrutinised after taking out duplicates for integrity and relevance according to Healthcare Scientists, Diagnostics/Screening, Primary Care. 7 papers were further excluded. 23 Full-Text articles further appraised for eligibility. 5 further excluded. Remaining 18 papers were included (refer fig.1). 5 themes were identified.
Conclusion: There is a need for a review of the current healthcare scientist workforce in the UK and consideration for these health professionals being available for CKD patients in primary care.
Keywords: CKD; Collaboration; Education

Paediatric nephrology in under-resourced areas

P3-499 - Community-acquired paediatric acute kidney injury in a resource-constrained setting: burden and short-term mortality outcome

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Background: Acute kidney injury (AKI) is known to complicate many common disease conditions. There is limited data on community-acquired AKI (CAAKI) in children in this environment. This study describes the burden of paediatric CAAKI in northern Nigeria, and the short-term mortality outcome.
Methods: It was prospective, observational study of children who presented for the first time and were admitted to the emergency paediatric unit (EPU) of Aminu Kano Teaching Hospital (AKTH). Basic demographic data was obtained. Each child had blood samples for serum urea, electrolytes and creatinine collected on admission. A second sample was collected after 12 hours. Urine output was monitored over the first 48 hours of admission. AKI was defined based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria. All children were followed up for 48 hours to observe mortality outcomes. Data analysis was done using the SPSS version 20.
Results: A total of 529 children (male = 295, 55.8%) were studied. Median (IQR) age was 36 (15, 84) months. Two-thirds (n = 347, 65.6%) were aged 60 months or less. AKI was present in 239 children (45.2%), 54 (22.6%) having severe (stage 3) AKI. Infants had an age-specific AKI prevalence of 64.4%. Almost half (47.5%) of the study population were admitted with severe malaria and sepsis. Other common diagnoses were bronchopneumonia (11.0%), meningitis (8.7%) and acute gastroenteritis (7.8%). Forty-one children (7.8%) died within 48 hours, sepsis and severe malaria accounting for over half of the deaths ($\chi^2 = 59.538$, $p = 0.003$). Of this number, 30 (73.2%) had AKI; 18 (60.0%) of this being severe. Derangement in serum potassium, low urea to creatinine ratio and presence of AKI using the urine output criteria were significant predictors of mortality.
Conclusion: Community-acquired paediatric AKI is common in this setting. Early identification with appropriately-timed intervention is necessary to prevent and reduce mortality.

Paediatric nephrology in under-resourced areas

P3-500 - Pattern of Renal Diseases in Children presenting to the Paediatric Nephrology Unit of Rivers State University Teaching Hospital, Nigeria: A 5 - year Retrospective Review

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Background: Renal disorders in childhood contribute to the growing burden of childhood morbidity and mortality in Nigeria. The pattern and burden of renal diseases is pertinent for planning, preventive and administrative purposes. This study aimed to determine the pattern of childhood renal diseases at the Rivers State University Teaching Hospital (RSUTH), Rivers state, Nigeria.
Methods: A review of case records of all children aged less than 18 years seen at the paediatric nephrology outpatient clinic over a period of 5 years (2015- 2019) were studied.
Results: A total of 10,372 children were seen during the study period with 140 of them having renal diseases, giving a prevalence of 1.3% (13 cases per 1000 children). There were 91 (65%) males and 49 (35%) females, with a male to female ratio of 1.86:1. The ages ranged between 2 weeks and 16 years. Nephrotic syndrome was the most common 45 (32.1%), followed by congenital anomalies of the kidney and urinary tract (CAKUT) 29 (20.7%), acute glomerulonephritis 27 (19.3%) and urinary tract infections 20 (14.3%). The top two congenital renal anomalies were posterior urethral valve 16 (11.4%) and ectopic kidneys 7 (5%).
Conclusion: Nephrotic syndrome and Acute glomerulonephritis were the most common acquired renal diseases whereas posterior urethral valve and ectopic kidney were the commonest congenital anomalies of the kidneys and urinary tract. The need for improvement of paediatric renal services and training of health workers to detect and managed these conditions are urgently needed.

Paediatric nephrology in under-resourced areas

P3-501 - Costs and Outcomes of Pediatric (COPE) CKD – Study design and interim results of a multicenter prospective health economics study from 3 low middle income countries (LMICs)

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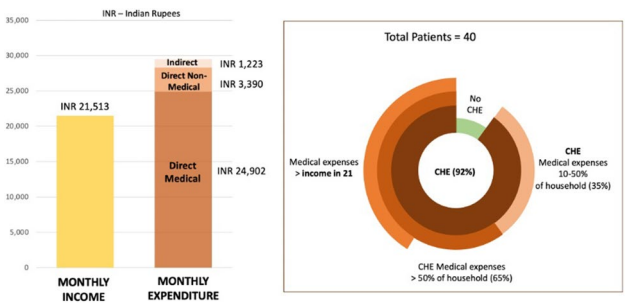
Introduction: Children with CKD have frequent discontinuation of treatment/death in LMICs. Pediatric nephrology centres are very limited and a mix of public (government covers costs) and private (patient pays out-of-pocket OOP) centers and treatment may be associated with high out-of-pocket (OOP) costs from a patient perspective.
This first, prospective health economics study of pediatric CKD in 3 LMICs aims to determine the frequency of catastrophic healthcare expenditure (CHE), direct and indirect healthcare OOP costs and rates of discontinuation of care/death.
Methods: CKD patients (1-18 years, CKD 3b,4,5) will beincluded in 7 centres -India (3 private/ 2 public), Bangladesh (1 private), Ethiopia (1 public).
Data collection: Clinical & sociodemographic details.
Healthcare OOP expenditure: Direct medical (dialysis, medicines, laboratory, hospital admissions/visits), Direct non-medical (travel, lodging) and Indirect costs (lost wages by caregivers)and school absence (patient).
Occurrence of CHE (WHO definition): monthly OOP healthcare expenditure > 10% of total household expenditure
Financial distress: taken loans/ sold belongings.
Discontinuation of treatment: No visits to centre 6 months without transition of care or Death.
Interim Results: All centres have obtained IRB approval and have begun enrollment.
PI centre(India): 40 patients, 32 (80%) in kidney failure, 30 on dialysis (70% manual PD). Figure 1 shows the direct healthcare OOP costs incurred vs monthly income and frequency/ magnitude of CHE. Financial distress occurred in 15 (42%). Caregivers lost avg 7% of monthly income and 17 (43%) discontinued schooling. Discontinuation of treatment/death occurred in 7 (18%), 16 (40%) were non-adherent with clinic visits or medications.
Centre 2(India): 42 patients, 19 (45%) in kidney failure. Only 9 (47%) receive maintenance dialysis. Frequency of CHE = 100%. Financial distress = 11 (26%) and 7 (17%) discontinued treatment/died.
Conclusions: The novel economic and outcome data from this study will inform advocacy for equitable access to pediatric CKD care and enable future targeted interventions to improve patient-centered outcomes in LMICs.



Paediatric nephrology in under-resourced areas

P3-504 - Paediatric screening and long-term follow-up of children and young people [CYAP] in Ginnoruwa, Sri Lanka - an established global 'hotspot' for adult chronic kidney disease of unknown origin [CKDu].

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Introduction: Significant albuminuria and positive urinary markers have been reported in paediatric cohorts in some CKDu-endemic global pockets. False positive results and lack of long-term data limit justification for routine paediatric screening. This study aims to identify and follow-up, long-term, paediatric kidney disease in an established adult CKDu-'hotspot' in Sri Lanka.
Method: A two-stage population-based long-term cohort observational study.
2018: CYAP[1-17 years] in CKDu-endemic Ginnoruwa[four-village radius in North-Central Sri Lanka] invited to a school-based screening study. Demographic data, birth weight[BW] current weight, height, blood pressure, urinalysis, renal function and baseline urinary tract ultrasound scan [USS] data were collected.
2022: Follow-up door-to-door study:CYAP with significant albuminuria in the first phase were clinically reviewed and re-screened for albuminuria. Careful attention was paid to collection methods and laboratory processing times to reduce the likelihood of false positive results. Urine was stored for future urine biomarker testing in those with persistent albuminuria. Final dataset was analysed via descriptive statistics and mean comparisons using SPSS(Version24).
Results: 400 CYAP attended the 2018 screening programme. 352 met inclusion criteria-176(50%) male; median age 8.12 years; mean BW 2.85kg; 35[n=352] had significant albuminuria ($p<0.001$)[mean ACR-126.71mg/g]. Mean serum creatinine and estimated GFR were 57.81µmol/L and 88.84ml/min/1.73m2 respectively. 8[n=352] had small kidneys or renal calculi on USS. 35 with albuminuria were followed up 4 years later. 1[n=34] had significant albuminuria; 1 lost to follow-up. 33[n=34] CYAP had no significant albuminuria(97.05%). The incidence of albuminuria on long-term follow up was significantly lower than the 2018 baseline($p<0.001$).
Conclusion: In contrast to existing research, this study found a significantly lower incidence of early kidney disease on long term follow-up of this large paediatric cohort in CKDu-endemic Ginnouruwa. Large cohort multinational collaborative studies are needed to validate and further understand this key finding. The presence of few USS abnormalities and the relatively lower median BW in this cohort remain noteworthy.

Paediatric nephrology in under-resourced areas

P3-505 - This is a case of lupus anticoagulant hypoprothrombinemia syndrome associated with a hemorrhagic ovarian cyst in a 17-year-old girl with systemic lupus erythematosus

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A 17-year-old girl with SLE presented with squeezing colicky abdominal pain for a day (2018.12). She had been diagnosed with SLE, based on ecchymosis and prolonged bleeding after tooth extraction at 9 years of age (2011.9). About one year later she developed proteinuria (10.7 mg/m^2/hr) and renal biopsy showed focal segmental proliferative lupus glomerulonephritis Class IIIA. At that time, the patient had positive results for the lupus anticoagulant (LA) and immunoglobulin G (IgG)/IgM anti-phospholipid antibodies with prolonged activated partial thromboplastin time (aPTT) and normal international normalized ratio (INR) (2012.10). She had taken a combination of mycophenolate mofetil (MMF), prednisolone, azathioprine, enalapril or hydroxychloroquine. On physical examination, her vital signs were within normal limits, and epigastric and generalized abdominal tenderness was found without hepatosplenomegaly. Coagulation studies revealed INR and aPTT prolongation and LA positivity. Levels of C3 and C4 were decreased. She had positive findings for anti-cardiolipin antibodies (aCL) IgG and anti-beta-2-glycoprotein I (β2GP1) IgG/IgM. Due to abdominal discomfort and suspected SLE flaring, MMF dose was reduced and steroid dose was increased. Three months later (2019.3), she complained of dizziness and menorrhagia. Red blood cell transfusion was performed at a hemoglobin level of 7.4 g/dL. Laboratory tests showed prolonged aPTT and INR, LA positivity, and positive findings for aCL IgG and anti-β2GP1 IgG/IgM again. Proteinuria was aggravated from 519 mg/day to 1,204 mg/day. Pelvic sonography showed decreasing sized ovarian cystic lesion (< 2 cm). For the control of menorrhagia, combined oral contraceptive pill was given for 3 months. Repeated coagulation studies showed persistently prolonged aPTT (the longest 106.8 sec) and low factor II level (the lowest 14%). A diagnosis of LAHPS associated with SLE was made. She received six courses of cyclophosphamide pulse therapy (monthly 6 times). After that, she is currently taking cyclosporine, prednisolone, hydroxychloroquine, and enalapril.

Paediatric nephrology in under-resourced areas

P3-506 - Kidney damage in unattended children with sickle cell disease admitted to the pediatric ward of two hospitals in Benin

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Introduction: Sickle cell disease is a chronic condition that affect all organs including the kidneys. The objectives of this work was to study kidney dammage during sickle cell disease in untreated children admited to pediatrics at CNHU-HKM and CHUD-OP.
Methods: This was a cross-sectionnal prospective descriptive and analytical study carried out a 3-month period(october to december 2019) in pediatrics departments at CNHU-HKM and CHUD-OP. We included children aged 6 months to 18 years with SS, SC sickle cell disease or Sb thalassemia. Data analysis was computer based.
Results: Fifty children were included with female predominance (54%). The sex ratio was 0.85. Seventy deux percent of the children were of the SS genotype while 28% were SC. The mean age was 125.84 months ±50.07. Forty-three children among the 50 included had kidney damage. Hyperfiltration was the most common renal disease (67.44%) followed par hyposthenuria (60.46%). None of the risk factors sought were statiscally associated with kidney damage in these patients.
Conclusion: Kidney damage is common during sickle cell disease and may be present already at a very young age.Only systematic screening can make it possible to discover it for early management . Regular follow-up of the sickle cell patientscan help prevent kidney damage or at least reduce its frequency.
Key words: Kidbey damge, sickle cell disease, childfen, Benin.

Alport syndrome (and other GBM diseases)

P3-510 - Clinical significance of digenic inheritance in Alport Syndrome

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Background and Aims: Alport syndrome (AS) is a genetically heterogeneous nephropathy. Digenic AS refers to the inheritance of pathogenic variants in two different of the three *COL4A3/COL4A4/COL4A5* genes and is associated with atypical presentations and more severe prognosis.The aim was to define frequency, clinical effects of an additional pathogenic variant in AS.

Method: We analyzed NGS-based genetic data of our AS cohort (n=108). Clinical (age of macrohematuria (MH), proteinuria (Pr), sensorineural deafness (SND), arterial hypertension (AH)), laboratory data (Pr,mg/m^2/day; eGFR,ml/min/1,73m^2) at the first and last presentations (FU=4[2;6] yrs) were compared in 2 groups:1st gr - pts with monogenic X-linked AS associated with missense variants (n=59, 33M), 2ndgr - pts with digenic (*COL4A5* missense variant+*COL4A3* or *COL4A4*) inheritance (n=6, 3M).

Results: Digenic AS variants had 7pts(q=0.06,4M/3F).There were no difference in the age at first presentation (8.1±4.3 vs 7.3±4.5yrs), age of MH (3.8±2.7 vs 2.3±0.4yrs), frequency and age of Pr (q_1=0.59 vs q_2=0.66, 6.8±4.4 vs 8.6±6.3yrs), AH (q_1=0.52 vs q_2=0.5, 10.8±3.8 vs 14.3±4.2yrs), SND (q_1=0.28 vs q_2=0.16, 8.5±4.9 vs 15yrs), eGFR decline (q_1=0.28 vs q_2=0.33, 11.7±3.6 vs 16yrs) between groups. Pts of 2ndgr more often had MH (q_1=0.28 vs q_2=0.66, p=0.020) and nephrotic range Pr (χ_2=5.193,p=0.023). The level of Pr and eGFR at the fist (169±47 vs 313±84 mg/m^2/day, 99±18 vs 103±17 ml/min/1,73m^2) and last presentations (334±74 vs 345±94 mg/m^2/day, 95±25 vs 100±19 ml/min/1,73m^2) were comparable. Girls of 2nd group more often had MH (0.66 vs 0.16,p=0.044), males with digenic inheritance had higher level of Pr at the fist presentation (565±145 vs 3230±46 mg/m^2/day, p=0.035) and nephrotic range Pr(χ_2=5.464, p=0.020).

Conclusion: About 6% of our pts have digenic AS inheritance. Digenic inheritance associates with MH in girls and more severe Pr in boys.

There limitations of the study are: small sample of pts, short follow-up, treatment with ACEi that will affect the pts prognosis.

Alport syndrome (and other GBM diseases)

P3-511 - Alport syndrome. Report of a family case

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Alport syndrome. Family case

Introduction: Alport syndrome presents an alteration of the glomerular basement membrane, secondary to a type IV collagen defect. Hereditary nephropathy presenting with hematuria, commonly associated with sensory deafness and/or ocular lesions. It is found in about 3% of children with Chronic Kidney Disease. Mainly linked to the X chromosome.

Clinical Case: Male, 2 years old, consulted for a change in urine color of 1 year of evolution, during all urination, without clots, Coca-Cola color, intermittent several times a month, without pain or fever. Background: Maternal uncle died of Chronic Kidney Disease on hemodialysis and maternal aunt on hemodialysis (both unknown etiology). Physical exam: Weight 12.5kg (P50), T: 90cm (P50-P25), BP 95/50 (P75), diuresis 2-3cc/kp/h, paleness, rest normal. Laboratory: normal blood count, renal function, electrolytes, EAB, complement (C3 and C4). ANA, AntiDNA, ASTO negative. Simple Urine: Proteins +++, Red Blood Cells >300xc. Negative urine culture. Pr/Cr index: 1.3; Normal Ca/Cr index. Normal kidney ultrasound. PBR: mild to moderate glomerular mensangial hypercellularity; negative immunoglobulins, complement and fibrinogen. Ophthalmology and Otorhinolaryngology, at the time of examination without alterations. Enalapril nephroprotection (0.2mg/kp/day). He abandoned follow-up and treatment, returns after 2 years with the same signs and symptoms, also accompanied by a brother who has hematuria and kidney failure requiring emergency dialysis, bilateral hearing loss. The diagnosis of Sx Alport is made based on symptoms, suggestive PBR and family history. Currently, the patient attends regular check-ups, with preserved kidney function and the brother received a kidney graft.

Discussion: When faced with a patient with hematuria and proteinuria, it is important to take a good history, investigate the relatives, in this case both parents without hematuria or proteinuria, but two maternal relatives with significant kidney disease. Although there is no genetic study, suspect Alport syndrome in order to carry out early treatment.

Alport syndrome (and other GBM diseases)

P3-512 - Kidney disease progression and risk factors in pregnant women with Alport syndrome

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Background: Whether pregnancy leads to the aggravation of kidney impairment in women with Alport syndrome (AS) is one of the most concerned issues in genetic counseling. Here we conducted a retrospective study of pregnant women with AS to provide clinical data on this topic.

Methods: The clinical data throughout pregnancy of women with AS, who underwent prenatal diagnosis from 2011 to 2021, were collected. AS stages were defined as follows: stage 0: microhematuria; stage I: microalbuminuria; stage II: overt proteinuria; stage III: decreased kidney function. Progression of AS was defined as the initial stage of AS progressed into next stage after delivery, or further decline in renal function. A multiple logistic regression was used to evaluate the risk factors of disease progression.

Results: A total of 52 women were enrolled, including 50 X-linked AS (XLAS) and 2 autosomal recessive AS (ARAS). The mean age of pregnancy was 32 years (range 22-40 years). The mean follow-up time was 4.71 years (range 0.61-14.12 years). Disease stage 0-I was most common before pregnancy (57.69%), whereas stage II occupied the highest ratio after delivery (42.31%; P<0.05). The rate of overt proteinuria and declined kidney function after delivery were significantly higher than that before pregnancy(P<0.05). The overall rate of disease progression was 42.31% (2 ARAS, 20 XLAS). In women with XLAS of stage 0-I and stage II-III before pregnancy, the rate of progression was 40.74% (11/27) and 36.84% (7/19; P>0.05), respectively. AS stage during pregnancy was the only risk factor of disease progression (p < 0.001).

Conclusion: This study confirmed there was a nonnegligible rate of kdney disease progression in pregnant women with AS, and AS stage during pregnancy is an independent risk factor for disease progression. This supports the need for close follow-up during pregnancy in all women with AS.

Alport syndrome (and other GBM diseases)

P3-513 - Clinical analysis of 30 children by gene diagnosis of Alport syndrome

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Objective: to investigate the clinical significance of the clinical phenotype and gene mutation detection in children with Alport syndrome.
Method: the data of 30 children with gene mutation admitted to Guangzhou No.1 People's Hospital from January 2013 to June 2017 were retrospectively analyzed. Collecting of peripheral blood samples from children and their family members .Then using gene sequencing exon sequence capture technology to find out whether there is mutation gene including IV type collagen alpha 3 chain (COL4A3), alpha 4 chain (COL4A4) or alpha 5 chain (COL4A5).And gene mutations of related family members were identified by Sanger method.
Result: 30 children with AS were diagnosed by gene detection. Renal biosy was performed in 18 cases of 30 children with AS,and the results of light microscopy were varied. Electron microscopic examination revealed diffuse thinning, thickening and delamination of the glomerular basement membrane (GBM) in 5 cases(16.67%). The electron microscopic examination shows thin basement membrane disease in 4 cases(13.33%). 3 cases (10.00%) of immunofluorescence shows type IV collagen alpha 3, alpha 5 chain negative in renal tissue. 22 cases were diagnosed X linkage dominant hereditary Alport syndrome (XL-AS) by gene text,finding 8 new mutation sites of COL4A5. Genetic diagnosis of 8 children with autosomal recessive inheritance, and 3 new COL4A4 mutations were found.
Conclusion: The clinical manifestations of children with Alport syndrome are diverse, lack of specificity, and the pathological types of renal tissue are different. It is difficult to diagnose early. Gene detection contributes to the early diagnosis of AS, to judge the prognosis of the children, and to avoid unnecessary drug treatment.

Alport syndrome (and other GBM diseases)

P3-514 - Lifetime risk of autosomal recessive Alport syndrome calculated from genetic databases

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Background: Alport syndrome (AS) is a rare hereditary nephropathy. It is characterized by microscopic hematuria followed by proteinuria leading to end-stage kidney failure (ESKF), sometimes associated with hearing loss and eye abnormalities. To date, prevalence estimations for hereditary nephropathies are mostly based on clinical diagnoses and do not consider patients with atypical symptoms. Studies on the basis of molecular genetic analyses to estimate the lifetime risk of AS are limited. The aim of this study was to estimate the lifetime risk for autosomal recessive Alport syndrome (ARAS) from genetic databases.
Methods: Using the publicly available databases ClinVar, HGMD, and LOVD, disease-causing variants (likely pathogenic and pathogenic variants as per the American College of Medical Genetics) in the genes *COL4A3* and *COL4A4* were collected. Their minor allele frequency was then assessed in the Genome Aggregation Database (gnomAD) and in our in-house exome database to estimate the lifetime risk.
Results: Overall, 425 disease-causing variants in *COL4A3* and 416 in *COL4A4* were investigated. The lifetime risk for the development of ARAS was estimated to be 0.35 in 100,000 individuals as calculated based on the in-house database. In gnomAD, the lifetime risk was estimated to be 0.34 in 100,000 and 0.44 in 100,000 in the European (non-Finnish) population and the global dataset, respectively.
Conclusion: We provide an estimation of the lifetime risk of autosomal recessive Alport syndrome based on molecular genetic data in different populations. The data will be essential for the identification of possible underestimated prevalences and therefore for resource allocation in therapy development and bio-medical research.

Alport syndrome (and other GBM diseases)

P3-515 - Very low-level somatic mosaic COL4A5 splicing variant is detected in an asymptomatic female using droplet digital PCR

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Background: X-linked Alport syndrome (XLAS) due to *COL4A5* disease-causing variants is a hereditary glomerulopathy featured by hematuria, proteinuria, and progressive renal failure. Very low-level (<1.0%) somatic mosaicism for *COL4A5* disease-causing variants has not been published.
Materials and Methods: Chinese XLAS families with suspected parental mosaicism were enrolled in the present study to evaluate the forms of mosaicism, to offer more appropriate genetic counselling. PCR and direct sequencing were used to detected *COL4A5* disease-causing variants harbored by the affected probands in parental multi-tissue DNAs (peripheral blood, urine sediments, saliva, hair), and droplet digital PCR (ddPCR) was used to quantify the mutant *COL4A5* allelic fractions in parental different samples such as peripheral blood, saliva and urine sediments.
Results: A Chinese asymptomatic female with suspected somatic and germline mosaicism was enrolled in the present study. She gave birth to two boys with XLAS caused by a hemizygous disease-causing variant c. 2245-1G>A in *COL4A5* (NM_033380) intron 28, whereas this disease-causing variant was not detected in genomic DNA extracted from peripheral blood leukocytes in the woman using Sanger sequencing. She had multiple normal urine test results, and continuous linear immunofluorescence staining of α2(IV) and α5(IV) chains of skin tissue. Sanger sequencing demonstrated that *COL4A5* disease-causing variant c. 2245-1G>A was not detected at her genomic DNAs isolated from urine sediments, saliva, and hair roots. Using ddPCR the wild-type and mutant-type (c.2245-1G>A) *COL4A5* was identified in the female's genomic DNAs isolated from peripheral blood, saliva, and urine sediments. The mutant allelic fractions in these tissues were 0.26% (peripheral blood), 0.73% (saliva), and 1.39% (urine), respectively.
Conclusions: Germline and very low-level somatic mosaicism for a *COL4A5* splicing variant was detected in an asymptomatic female, which highlights that parental mosaicism should be excluded when a *COL4A5* presumed *de novo* disease-causing variant is detected.

Alport syndrome (and other GBM diseases)

P3-516 - Spectrum of COL4A-nephropathy in an Indian cohort

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Introduction: Widespread availability of next-generation sequencing has enabled recognition of COL4A-mediated nephropathies in clinical settings other than typical Alport syndrome (AS).

Methods: We reviewed records of children who were diagnosed with COL4A-nephropathy based on next-generation sequencing. Variants on clinical exome sequencing were categorised using ACMG 2015 criteria. Where available, renal histology was reviewed.
Results: We found 31 variants (18 missense, including 7 intronic variants, and one large deletion and duplication, each) in COL4A5 (n=22), COL4A4 (n=6), and COL4A3 (n=3) in 34 patients (27 boys) with a median age at diagnosis 10.5 years (**Table 1**). AS was the clinical diagnosis in half, while one-third of patients were initially diagnosed with steroid-resistant nephrotic syndrome (SRNS). COL4A-nephropathy was suspected for persistent microscopic hematuria (n=3) with nephrotic-range proteinuria and non-response to immunosuppression (n=5), changes in glomerular basement membrane (n=4), hearing loss (n=5), kidney dysfunction (n=5), and/or family history (n=1). 24 patients (20 boys) had X-linked disease; 7 and 3 patients had autosomal recessive and autosomal dominant disease. Eleven patients presented with renal dysfunction, and nine progressed to end-stage kidney disease. Six of the latter had severe (nonsense/frameshift/splice site) mutations. Renal histology (n=22) showed focal segmental glomerulosclerosis, minimal change disease, and mesangial proliferation in similar proportions of cases on light microscopy. Electron microscopy, available in 14 patients, showed focal (n=12) or diffuse (n=1) glomerular basement membrane thinning in 13 patients, along with characteristic lamellation or rarefaction in ten cases; three patients had isolated membrane thinning. Eight patients had focal foot process effacement, including five patients presenting with nephrotic syndrome. Seventeen children had high-frequency sensorineural hearing loss, while one had lenticonus.
Conclusions: COL4A-nephropathies have varied clinical phenotype ranging from asymptomatic urinary abnormalities to typical AS and nephrotic syndrome.

Table 1. COL4A variants in the study

Gene	Variant (codon change; protein change)	Zygosity	Prediction	Presentation	Novelty
COL4A5	Exon 2; c.136G>T; p.Glu46Ter	Hemizygous	Pathogenic	H, P, NS, HL	-
	Exon 11; c.634del; p.Pro212fs	Hemizygous	Pathogenic	H, P, SRNS, K	-
	Exon 13; c.758_761del; p.Val253GlyfsTer92	Heterozygous	Pathogenic	H, P, K	Novel
	Exon 14; c.796C>T; p.Arg266Ter	Hemizygous	Pathogenic	H, P, K, HL	-
	Intron 20; c.1339+1G>T; 5'splice site	Hemizygous	Pathogenic	H, P	-
	Intron 24; c.1779+2T>G; 5'splice site	Hemizygous	Pathogenic	H, P	-
	Exon 46; c.4063del; p.Glu1355AsnfsTer22	Hemizygous	Pathogenic	H	Novel
	Exon 49;c.4341del; p.Gly1448ValfsTer106	Hemizygous	Pathogenic	H,P, K	-
	Exon 49; c.4480del; p.Ser1494Leufs*60	Hemizygous	Pathogenic	H, P	Novel
	Intron 52; c.4994+1G>A; 5'splice site	Hemizygous	Pathogenic	H, P, HL	Novel
	Exon 53; c.5020C>T; p.Arg1674Ter	Hemizygous	Pathogenic	H, P, K, HL	-
	Exon 3-30; del c.(141+1_142-1)_(2509+1_2510-1); deletion	Hemizygous	LP	H, P, K, HL	-
	Exon 22; c.1443C>A; stop gain	Hemizygous	LP	H, P, SRNS	Novel
	Exon 24; c.1634G>A; p.Gly545Asp	Hemizygous	LP	H, P, SRNS, K, HL, E (cataract)	-
	Exon 38; c.3446G>A; p.Gly1149Asp	Hemizygous	LP	H, P, HL	Novel
	Exon 41; c.3695G>A; p.Gly1232Asp	Hemizygous	LP	H, P, K	Novel
	Exon 53; c. (4994+1_4995-1)_(*1_?) dup; duplication	Heterozygous	LP	H, P, SRNS, K	-
	Exon 52; c.4862 C>T; p.Ala1621Val	Hemizygous	VUS	H, P, SRNS, K	-
	Exon 24; c.1677C>A; p.Asp559Glu	Heterozygous	VUS	H, P, SRNS, K	Novel
	Exon 48; c.4247G>A; p.Arg1416His	Hemizygous	VUS	H, P, SRNS	-
	Exon 20; c.1258G>A; p.Gly420Arg	Heterozygous	VUS	H, P	Novel
	Intron 32; c.2767+3A>G; 5'splice site	Hemizygous	VUS	H, P, NS, K, HL	Novel
COL4A4	Exon 39; c.3655C>T; p.Gly1219Ter	Compound heterozygous	Pathogenic	H, P, SRNS, K, HL	Novel
	Exon 25; c.1921C>T; p.Arg641Ter	Compound heterozygous	Pathogenic	H, P, SRNS, K, HL	-
	Exon 41; c.3933C>G, p.Tyr1311Ter	Homozygous	Pathogenic	H, P, NS	Novel
	Exon 46; c.4413_4414delCA; p.His1471GlnfsTer21	Homozygous	Pathogenic	H, P, K, HL	-
	Exon 39; c.3622del; p.Leu1208Ter	Homozygous	LP	H, P, SRNS, HL	Novel
	Intron 33; c.3151-8A>G; 3'splice site	Homozygous	VUS	H, P, K, HL	-
COL4A3	Exon 33; c.2702G>G/A; p.Gly901Asp	Heterozygous	LP	H, P	Novel
	Intron 24; c.1575+5G>C; 5'splice site	Homozygous	VUS	H, P, K, HL, E (lenticonus)	Novel
	Exon 18; c.1021C>A; p.Arg341Ser	Heterozygous	VUS	H, P	Novel

E: eye abnormality, H: hematuria, HL: hearing loss, K: impaired kidney function, LP: Likely pathogenic, NS: nephrotic syndrome, P: proteinuria, SRNS: steroid resistant nephrotic syndrome, VUS: variant of unknown significance

Alport syndrome (and other GBM diseases)

P3-517 - Variants of the CFHR5 gene in patients with Alport syndrome and IgA deposition in renal tissues

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Introduction: IgA deposition in the renal tissues has been found in some patients with Alport syndrome (AS). Variants of the *CFHR5* gene are identified in some patients with IgA nephropathy. Whether or not variants of the *CFHR5* gene is the cause of IgA deposition in renal tissues in the patients with AS is not known.
Materials and Methods: Clinical data, laboratory results, renal biopsy histopathology and whole exome sequencing results of the patients with AS were collected. According to IgA deposition in the renal tissues, the patients with AS, in whom IgA nephropathy and Henoch-Schonlein purpura nephritis were excluded, were divided into two groups: Group A and Group B. Variants of the *CFHR5* gene in patients with AS were retrospectively analyzed.
Results: Eleven patients with AS, in whom both renal biopsies and whole exome sequencing were performed, were included in the study. Group A had four AS patients with IgA deposition in renal tissues, and Group B had seven AS patients without IgA deposition in renal tissues. Three patients in Group A carried a variant of the *CFHR5* gene, c.508G>A (p.V170M), c.508G>A (p.V170M), c.491G>A (p.S164N), respectively, whereas only one patient in Group B carried the variant of the *CFHR5* gene, c.508G>A (p.V170M).
Conclusions: Variants of the *CFHR5* gene might be the cause of IgA deposition in renal tissues in patients with AS.
Keywords: Alport syndrome, IgA deposition, *CFHR5* gene, IgA nephropathy, Henoch-Schonlein purpura nephritis

Neonatal nephrology

P3-518 - The renal consequences of prematurity - are we screening adequately

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Introduction: Prematurity increases risk for renal impairment due to lower nephron number. Exposure to hypoxic damage, hemodynamic changes, nephrotoxic medications increases risk for glomerular and tubular damage. Early onset hypertension, elevated creatinine and proteinuria may be markers of sequelae. Measurement of renal volume rather than size and serum uromodulin a marker of nephron endowment may be indicators of renal consequences.
Aims: To study the impact of prematurity on renal size and volume in early childhood and its effect on glomerular and tubular function. To study serum uromodulin and its correlation with renal function.
Methodology: This cross-sectional study was performed on children born preterm between January 2014- December 2016 who were called between January and December 2019. Blood pressure measurements, proteinuria, creatinine clearance calculation and mean kidney volume (MKV) was calculated by renal ultrasound. Serum uromodulin was estimated by EUROIMMUN ELISA kit.
Results: Mean age for 37 children was 5.8 years;35% (13/37) of children had BP at 90th centile, 3/37 (7%) had pre-hypertension and 5/37 (14%) had stage 1 hypertension. Twenty children (20/37, 54%) had eGFR between 90-120 ml/min/1.73m^2; none had pathological proteinuria. There was no correlation between gestational age and renal parameters. MKV was 34.86 ± 8.64 ml, with lower MKV for GA< 28-33 weeks **(p=.0.05).** Mean serum uromodulin was 62.10 ± 45.84 ng/ml.;Low levels had linear relationship with hypertension and eGFR(p= 0.8 and 0.5)). Correlation between uromodulin levels <60 ng/ml and reduced MKV was significant **(p=0.002**). At uromodulin cut off < 52 ng/ml, there was significant reduction of MKV (<32 ml) (AUC 0.715, p**=0.02.)**
Conclusion: Preterm-born children are at risk of developing hypertension. Mean kidney volume rather than size is an early useful screening parameter. Lower serum uromodulin correlates with lower GA and mean kidney volume both of which can be useful markers for assessing the risk of renal insuffiency.

Neonatal nephrology

P3-519 - Should we heparinise in neonatal renal vein thrombosis (RVT)? A single paediatric tertiary centre experience.

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Objective: Management of neonatal RVT is varied with limited data regarding conservative versus heparin management. Heparin may reduce RVT progression but has associated haemorrhagic risks with debatable impact on renal outcome. We evaluated our management and outcomes of neonatal RVT over a 10-year period.
Method: Single centre retrospective study for all neonatal (<1 month old) RVT ultrasound confirmed cases between 2011-2021.
Results: 19 neonates had RVT – 84% male, 36% <37 weeks gestation. Median age at diagnosis of 3 days (range 1-30). 57% of patients had inferior vena cava (IVC) clot extension. 69% of neonates received heparin, 5% received tissue plasminogen activator and 26% were untreated. Median treatment time was 3 months (range 6 weeks- 6 months). 26% died prior to discharge -all with bilateral RVT. One had progression of intraventricular haemorrhage after commencing heparin and care was therefore withdrawn.
Of the survivors, in the heparin treated group 81% had affected kidney atrophy and only 18% had normal kidney ultrasonic findings. In the untreated cohort, 66% had an involuted kidney and 33% had normal kidney ultrasonic findings of affected side. There was no significant difference between the two groups (p=0.57).
At latest follow up for 7 children, CKD was prevalent with eGFR ranging between 55- 96ml/min/1.73m2 (median age 12 months). No patients developed hypertension or proteinuria.
Conclusion: Most neonatal RVT cases were treated with heparin. Despite this, 81% of affected kidneys atrophied and outcomes were similar for those treated conservatively. Nevertheless, heparin may have a role in preventing clot extension to the IVC and contralateral kidney. Known associated risks with heparin include haemorrhage – of which we report 1 case with a neonate who already had severe intraventricular haemorrhage. Clinicians should consider heparin use given the likely structural and functional outcomes of the affected kidney.

Neonatal nephrology

P3-521 - Association of birth weight and renal function in term and late preterm newborns

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Background: Very low birth weight (LBW) is a factor for developing chronic kidney disease (CKD). However, little is known about how the degree of LBW affects renal function in term and late preterm newborns.
Methods: We collected medical records of healthy infants who were delivered by cesarean section between 1 February 2020 and 31 January 2021 at Omihachiman City Medical Centre. The patients were divided into two groups according to whether they were term (birth at ≥ 37 weeks' gestation) or preterm infants. We then divided these groups into two more groups according to whether they had a normal birth weight (≥ 2500 g) or LBW (< 2500 g). Serum creatinine (sCr) concentrations were measured at day 3 after birth.
Results: One-hundred fifty-four patients met the inclusion criteria. The mean sCr concentration in the preterm and LBW group (n = 21, gestational age: 35.29 ± 0.76 weeks, birth weight: 2095 ± 215 g) was significantly higher than that in the preterm and normal birth weight group (n = 13, gestational age: 35.77 ± 0.58 weeks, birth weight: 2798 ± 246 g) (0.63 ± 0.08 vs 0.56 ± 0.10 mg/dL, p = 0.03). However, the mean sCr concentration in the term and LBW group (n = 28, gestational age: 37.10 ± 0.31 weeks, birth weight: 2281 ± 164 g) was not significantly different compared with that in the term and normal birth weight group (n = 92, gestational age: 37.75 ± 1.18 weeks, birth weight: 2989 ± 334 g) (0.60 ± 0.14 vs 0.54 ± 0.11 mg/dL, p = 0.106).
Discussion: Preterm infants, even those with a relatively low birth weight of approximately 2100 g, show significantly higher sCr concentrations than those with a normal birth weight at day 3. A relatively low birth weight might be a factor of developing CKD.

Nephrotic syndrome

P3-522 - A rare cause of high level proteinuria

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Background and Aims: Proteinuria can be a manifestation of various diseases. We present a patient with nephrotic range proteinuria due to a lymphatic system malformations.
Method: Clinical, laboratory and morphological data of patient were analyzed.
Results: 16-years old male was examined due to increasing proteinuria and hematuria discovered by chance a year earlier. His family history and clinical status were unremarkable excluding episodes of cloudy urine. The patient had nephrotic range proteinuria (8.2-3.8 gr/day) presented by albumin (78%), hematuria (71 cells/power fields) and leukocyturia (7 cells/power fields), low-normal albumin (30-31 gr/l), low IgG (4.85 gr/l), normal C3/C4 complement activity in blood; eGFR was 75 ml/min/1.73m^2 (Schwartz bedside). AntiHCV, antiHBcore-Ag, HBsAg, ANA antibodies were negative. Urine excretion of calcium (Ca/Cr=0.31 mmol/mmol), urate (Ur/Cr=0.18 mmol/mmol), oxalate (Ox/Cr=0.01 mmol/mmol), phosphate (P/Cr=2.1 mmol/mmol, TmP=1.36) examined for "very cloudy with unidentified crystals urine" was normal. The hypoechoic cystic mass without blood flow in the area of posterior bladder's wall was seen in US. Cystoscopy, MRI with contrast did not revealed pathology including

signs of lymphoproliferation and neoplasia. The kidney biopsy showed normal tissue (LM), negative IgA, IgM, IgG, C3, fibrinogen immunofluorescence; there were small unspecific deposits in GBM and focal podocytes processes effacement (EM).
After kidney biopsy turbid white urine was noted. There were lymphocytes, high levels of protein (5 g/l) and triglycerides (1,99 mmol/l in urine vs 0,99 mmol/l in blood) in urine and low blood albumin level (29 g/l). The T2-weighted MRI of the kidneys and retroperitoneum showed a cystic dilation of the lymphatic vessels in the region of the right kidney hilum extending along the aorta to its bifurcation.
Conclusion: We have demonstrated a rare case of chyluria as a cause of proteinuria and the need of visual evaluation of the urine in patients.

Nephrotic syndrome

P3-524 - Impact of COVID-19 on family wellbeing and quality of life among children with nephrotic syndrome during the first pandemic wave: results from the INSIGHT Study

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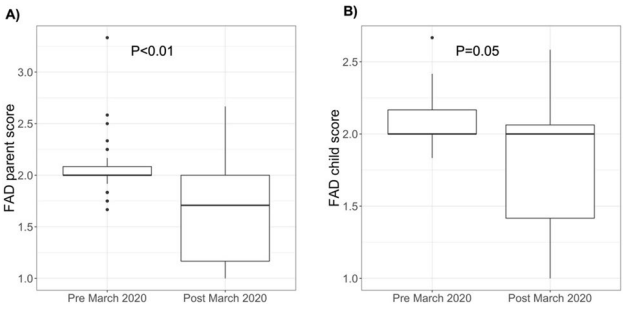
Background: During the global pandemic caused by severe acute respiratory syndrome coronavirus (SARS- CoV-2), one of the longest lockdowns in 2020 (5 months) worldwide was in Ontario. There are limited data available on the psychosocial wellbeing during the lockdown of parents and children with a chronic disease, potentially at risk for COVID-19.
Methods: A survey was conducted in 122 families with at least one child enrolled in the prospective cohort of childhood nephrotic syndrome (Insight into Nephrotic Syndrome [INSIGHT] Study) aged 2-18 years at the Hospital for Sick Children in Toronto, Ontario with available data pre-pandemic. Validated measures of wellbeing included McMaster Family Assessment Device (FAD) for parents and children ≥ 12 years to assess family dynamics, Patient Health Questionnaire for Depression and Anxiety (PHQ-4) for parents and Pediatric Quality of Life Inventory (PEDSQL™-V4)-either parent- or child-reported depending on age. Families completed study questionnaires annually, and a subset, (n=107 families), completed repeated questionnaires prior to the pandemic and survey from August 21 – December 10, 2020. Wellbeing scores were compared and analyzed in this subset using the Student's t-test or the Mann-Whitney U test, as appropriate.
Results: Among the 122 children, 71% were male, and mean age at survey completion was 7 years old. In the subset, parents and children reported that family dynamics improved during COVID (Figure 1), compared with pre-COVID (parent: p<0.01; child: p=0.05). Children's overall HRQOL declined (p=0.04). Sleep was disrupted (p=0.01) and was worsened with increasing child age (β=–1.6 (IQR: -2.6, -0.67)). Overall QOL was lower in older children (β=-1.0 (IQR: -1.7, -0.2)).
Conclusions: Despite the positive effects of family dynamics, there was evidence of negative effects of sleep disruptions and reduced quality of life on the overall wellbeing during the lockdown compared to before the pandemic.



Nephrotic syndrome

P3-525 - Serum Tumor Necrosis Factor-Alpha (TNF-α) levels in children nephrotic syndrome with proteinuria

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Heavy proteinuria is the cardinal sign of nephrotic syndrome. The presence of proteinuria induced inflammatory reaction that further may increase chronic kidney disease progression. Tumor necrosis factor α (TNF-α) is one of cytokine has a role to exerts inflammation, proteinuria and may cause kidney damage.
The purpose of this study was to evaluate the association between serum TNF- α levels and proteinuria in children with nephrotic syndrome.
Methods: Analytical observational cross sectional design study was conducted in out patients clinic pediatric nephrology Dr Soetomo Hospital from January to April 2021. The population of the study were children with nephrotic syndrome the age lest than 18 years. The variable of the study were the levels of serum TNF-α, urine albumin creatinine ratio (uACR) ≤ 30mg/gCr, uACR 30-2220 mg/gCr, >2220mg/gCr, nutritional status, glomerular filtration rate (GFR), diagnosis nephrotic syndrome (NS) (nephrotic syndrome initial attack, nephrotic syndrome dependent steroid-NSDS, nephrotic syndrome frequent relapse-NSFR, nephrotic syndrome resistance steroid- NSRS), acute kidney injury (AKI). The statistical analysis using Kruskall-Wallis.
Results: Total 70 children with NS included in this study. The main population was male 47 (67.1%) with the age mean 9.1 ± 4.7 years. The median serum of TNF-α levels in uACR ≤30mg/gCr was 25 (17.1-46.2); Serum TNF-α levels in uACR >30-2220 mg/gCr was 27.6 (14.8-521.5)pg/ml; Serum of TNF-α levels in uACR >2220 mg/gCr was 24.7(12.5-270.3)pg/ml. There were no significant differences between serum of TNF-α levels with the degree proteinuria (P>0.05). And there were also no significant differences between nutritional status, diagnosis NS, AKI and serum of TNF- α levels (P>0.05).
Conclusion: The serum of TNF-α levels were not depends on the degree proteinuria.
Key words: serum of TNF-α, nephrotic syndrome, proteinuria

Nephrotic syndrome

P3-527 - Urinary vitamin D-binding protein levels in idiopathic nephrotic syndrome children."-a cross sectional study

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Background: Nephrotic syndrome (NS) is a common chronic kidney disease in childhood and it is mostly idiopathic. Idiopathic nephrotic syndrome (NS) associated with increased urinary vitamin D-binding protein (uVDBP) excretion. we conducted this study to evaluate the early and non-invasive method to diagnose steroid resistant nephrotic syndrome children by urinary vitamin D-binding protein levels and to co-relate urinary vitamin D-binding protein in biopsy proven FSGS children.
Settings and Design :It is a cross-sectional study carried out in 61 patients who had idiopathic nephrotic syndrome presented to Pediatric department of Dr Prabhakar Kore Hospital & MRC Belagavi, Karnataka, India. Urine and clinical data were collected from patients. Measurements of UVDBP were performed with a commercially available ELISA kit(R&D systems).
Demographic and Bopsy data:

	SSNS	SRNS
Age (Mean)	6.6yr	9.7r
Sex (M/F)	33/18	7/3
Biopsy	FSGS:11% (6)MCD: 5.8% (3)Others: 23% (12)No Biopsy: 58% (30)	FSGS: 40% (4) MCD:10% (1)Others: 50% (5)

Results: A mean UVDBP value of 4250ng/ml was observed in all the steroid resistant nephrotic syndrome patients with a sensitivity of 85.7% and a specificity of 84.0% for the samples tested, a linear line achieved on the standard curve with R2 value of 0.984.A mean uVDBP value of 308ng/ml was observed in all the steroid sensitive nephrotic syndrome patients.
Conclusion: UVDBP represents a non-invasive biomarker that could distinguish steroid resistance from sensitive in nephrotic children.●●No positive co-relation was observed between the biopsy and the uVDBP levels in Nephrotic children.

Nephrotic syndrome

P3-528 - Dysregulation of T-cell metabolism in patients with steroid-resistant nephrotic syndrome

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Early relapse following rituximab in patients with minimal change disease is associated with baseline reduction in regulatory T-cells and T-cell hyporesponsiveness. This study aimed to delineate mechanism of T-cell hyporesponsiveness and its association to metabolic alterations in patients with steroid-dependent (SDNS) and steroid-resistant nephrotic syndrome (SRNS).
48 patients with childhood-onset SDNS (n=31) and SRNS (n=17) were recruited during relapse. Patients with genetic causes were excluded. T-cell activation assay was performed on whole blood while metabolomic profiling was performed on purified stimulated CD4 T-cell culture supernatants (n=23) using GC-MS/MS and analysed using Shimadzu Smart Metabolites Database. Differences in the metabolomic profiles were identified using PLS-DA (SIMCA), and pathway analysis was performed using MetaboAnalyst 4.0. Real-time PCR was subsequently used to quantify the expression of key enzymes in identified pathways.
T-cell activation was muted in SRNS compared to SDNS patients with lower expression of CD69 (88±2.3% vs 91±3.1%, P=0.024) and IFNγ (1.9±0.73% vs 6.6±1.35%, P=0.016). 93 metabolites were identified in CD4 supernatant, and PLS-DA modeling yielded one fitted component, in which 24% of the variability in metabolites measured (R^2X) could explain 58% of the variation in steroid-response (R^2Y). Of note, 85% of the metabolites tended to be lower in SRNS compared to SDNS patients, and pathway analysis implicated mainly biosynthetic pathways e.g. glyoxylate and dicarboxylate metabolism (Benjamini-Hochberg P<0.05). Interestingly, the two metabolites with the highest VIP score (threitol and erythritol) were downstream products in the pentose phosphate pathway and were reduced in SRNS compared to SDNS patients (P<0.001). This was associated with downregulation of ribulose-5-phosphate-3-epimerase (RPE), a key enzyme in the pentose phosphate pathway, in SRNS compared to SDNS patients ($4x10^{-4}$±$2x10^{-5}$ vs $5x10^{-4}$±$3x10^{-5}$, P=0.014)
T-cell hyporesponsiveness to *in vitro* stimulation in SRNS patients was associated with metabolic quiescence, evidenced by dysregulated biosynthetic pathways including the pentose phosphate shunt.

Nephrotic syndrome

P3-529 - Long-term outcomes of repeated rituximab therapy to maintain remission in children with frequently-relapsing, steroid-dependent nephrotic syndrome: an international multi-centre study

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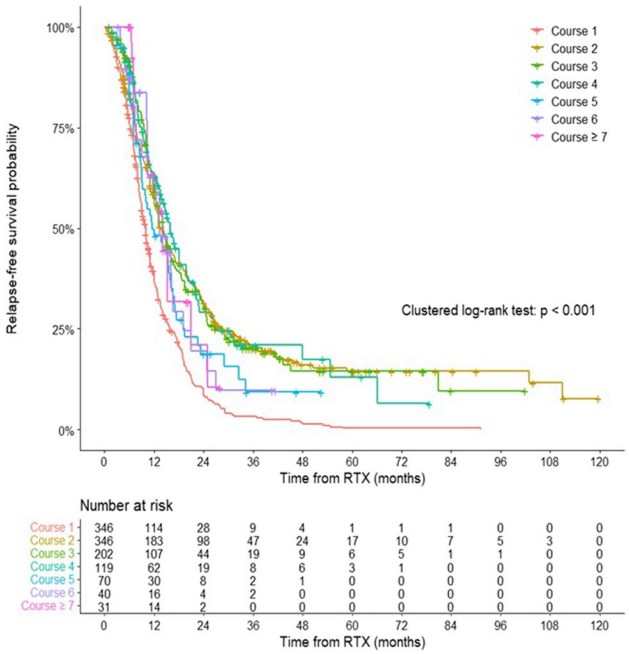
Background: Children with frequently-relapsing, steroid-dependent nephrotic syndrome (FRSDNS) often require multiple courses of rituximab. The aim of this study is to evaluate long-term outcomes in these children following repeated rituximab.
Method: We conducted an international, multicentre, retrospective cohort study at 16 paediatric nephrology centres from 9 countries in Asia, Europe and North America. All children with FRSDNS who received ≥2 courses of rituximab by 21 years, between 2005-2020, were included. Each rituximab course consisted of a total dose ranging from 375-1500mg/m2, with or without concurrent immunosuppression. Primary outcomes were relapse-free survival and adverse events.
Results: 346 children (age 9.8 years, IQR 6.6-13.5; 73% boys) received 1154 rituximab courses. A total of 144, 83, 49, 30, 21 and 19 children received 2, 3, 4, 5, 6 and ≥7 courses, respectively. Median relapse-free period overall was 12.4 months (95% CI, 11.9-13.1). Median follow-up duration was 5.9 years (IQR, 4.3-7.7).
Relapse-free survival differed by treatment courses (clustered log-rank test $P<.001$). Compared to first course (10.0 months, 95% CI, 9.0-10.7), relapse risk progressively decreased following subsequent courses (adjusted hazard ratio, HR_{adj}, 0.04-0.17; 95% CI, 0.02-0.22; $Ps<.001$), with the longest relapse-free period following fourth course (16.2 months, 95% CI, 12.0-16.0). B-cell depletion duration remained similar with increasing number of treatment courses (6.1 months, 95% CI, 6.0-6.3).
Most adverse events were mild. Although 51% treatment episodes with immunoglobulin monitoring (n=354/697) developed hypogammaglobulinaemia, only 79 episodes were considered clinically significant with either very low IgG levels (<200mg/dL), concurrent infections and/or need for immunoglobulin replacement. There were 42 (3.7%) and 18 (1.6%) episodes of neutropenia and agranulocytosis. 48 patients developed 52 infections and incidence was similar between treatment courses.
Conclusion: Children receiving repeated rituximab experience an improving clinical response. Side effects appear acceptable even after multiple courses but significant
complications do occur. These findings support repeated rituximab use in FRSDNS.



Nephrotic syndrome

P3-530 - Evaluation of Association Between UMOD Gene Variants and Renal Outcomes in Children with Nephrotic Syndrome

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In recent genome-wide association studies have identified common variants in the uromodulin (UMOD) gene relating to eGFR and risk of chronic kidney disease.
Aim: In this study, we aimed to explore associations of UMOD gene variants with renal outcome and clinical findings in children with nephrotic syndrome (NS).
Methods: The children with NS were enrolled in this study. Demographic characteristics, clinical and laboratory data, and presence of UMOD rs12917707 and rs11864909 variants of children were evaluated. The patients were classified as 3 groups according to their kidney functions: Group 1 children with end stage renal disease (ESRD), Group 2 children with eGFR <90 with or without proteinuria (CKD), Group 3 children with eGFR>90 (remission).
Results: A total of 120 children, 73 boys (60.8%), median age at diagnosis 65.88±45.06 months, median follow-up 82.93±54.97 months, were included in the study. There were 36, 15 and 69 children in groups I,II and III, respectively. In the group 1 (ESRD), it was found that median age at diagnosis was higher, the follow-up period was longer, the rate of consanguinity between the parents was higher, and

the rate of presence of NS in the family was more frequent (p<0.05). The pathological allel distributions of the UMOD rs12917707 and rs11864909 variants were found to be similar in the patient with steroid-resistant, steroid-sensitive, steroid-dependent, frequently relapsing and complete remission NS subgroups. UMOD gene rs11864909 pathological variant distribution was found to be higher in group 1 (ESRD) than the others (p=0,04). Similarly rs11864909 pathological variant distribution was higher in patients with steroid resistant NS and ESRD than the others (p=0.03). And also rs11864909 pathological variant distribution was higher in patients with hematuria at diagnosis than the others (p=0,003)
Conclusion: Our results suggest that UMOD gene rs11864909 variant may be associated with the renal outcomes in children with NS.

Nephrotic syndrome

P3-531 - The VExUS protocol in nephrotic syndrome

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Purpose: To define the effectiveness of the application of the VExUS ultrasound protocol in the volemic assessment of nephrotic patients.
Materials and Methods: The VExUS (Venous Excess Ultrasound Score) protocol, was recently proposed to evaluate and scores the severity of venous congestion, using a color-doppler ultrasound. It is divided in four steps. The first one evaluates the inferior vena cava (IVC), which, however, in pediatric patients is an inaccurate parameter, due to technical limitations and confounding factors (respiratory variability, heart disease). The others step evaluates Doppler analysis of the portal vein, suprahepatic veins and intrarenal interlobar veins. For each parameter a severity score is established with a score from 0 to 3. In our study we enrolled children with a nephrotic syndrome (NS). The VExUS analysis was performed at the admisson and at discharge of patients.
Results: We performed VExUS protocol in four patients (2 girls), with an average age of 6.2 year. Two children had a relapse of NS. We found a score of 1 in three children and a score of 2 in one patient at the admission. We repeated VExUS at discharge, with a range from 8 to 14 days later, and the score was zero in all the patients.
Conclusions: The VExUS score is a new system of evaluation and grading of volemic status. In our experience it is a rapid, safe, non-invasive and inexpensive ultrasound protocol that allows an early diagnosis of venous congestion. We proposed to use this score in children with NS especially in children with relapses of NS, in which the hypervolemia is not clinically manifested yet. Moreover, it can represent a guide to achieve the best possible therapeutic result, avoiding over- or under-treatment.

Nephrotic syndrome

P3-532 - Ofatumumab for Multidrug-Resistant Nephrotic Syndrome in Children: A case Series

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Background: Ofatumumab is a humanized anti-CD20 monoclonal antibody that is currently used off-label for childhood nephrotic syndrome. We report our center's experience with administering ofatumumab to three pediatric patients with idiopathic nephrotic syndrome (NS).
Methods: In 2021, three patients were treated with ofatumumab. All three patients had multi drug resistant nephrotic syndrome in their native kidneys. All the children had the clinical diagnosis of idiopathic NS (edema; urine protein/creatinine ratio > 2 mg/mg, or 3+ protein on urine dipstick; and hypoalbuminemia ≤ 2.5 g/dL, without evidence of secondary cause's with minimal changes on their kidney biopsies. We followed the same dosing protocol based on the report by Basu et al, with a first dose of 300 mg/1.73m^2 followed by 5 weekly doses of 2000 mg/1.73m^2
Results: Patient X and Y presented with steroid dependent nephrotic syndrome at 2.5 and 2 years of age. Their nephrotic syndrome was resistant to Tacrolimus, Mycophenolate Mofetil, Azathioprine and Rituximab. Within a week of starting ofatumumab, they began to show signs of improvement with spontaneous diuresis and decreased weight. They were in near complete remission by the end of therapy and continue to be in remission at the time of this report. (10 and 6 months post completion of treatment).
Patient Z presented with steroid dependent NS at 3 years of age. His nephrotic syndrome was resistant to Tacrolimus, MMF, Azathioprine and Rituximab and subsequently developed an allergic reaction to Rituximab. Despite completion of six doses of ofatumumab, he continued to have nephrotic syndrome with persistent in nephrotic-range proteinuria, hypoalbuminemia and edema. In all the three patients, the whole B-cell compartment was reduced to zero with CD19+ cells depleted to 0 % (absolute CD19 count <25 cells/mm^3).
Conclusions: Ofatumumab may be a treatment option for refractory childhood nephrotic syndrome.

Nephrotic syndrome

P3-533 - Profile of acute kidney injury among childhood nephrotic syndrome

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Introduction: There is paucity of literature on profile of Acute Kidney Injury (AKI) among childhood nephrotic syndrome (cNS).
Aims & Objective: To prospectively study the profile of AKI in cNS.
Methods: Prospective multicenter observational study was conducted from September 2020 to August 2021 wherein children (1-18 yrs) admitted with NS without any nephritic features or pre-existing chronic kidney disease were recruited.
Results: We screened 265 admissions with cNS of which 200 met the inclusion criteria [63% female, median age 4(IQR: 3-7) years]. AKI as per KDIGO serum creatinine criteria was seen in 36 (18%) admissions [81% male (n=29), median age = 3.7(IQR: 2-7) years, Stage I – 17% (n=6), Stage II – 78% (n=28) and Stage III – 6% (n=2)]. Multivariate analysis showed male gender, serum albumin </= 1.4 g/dl (OR 4.35; 95% CI 1.55 – 12.8; p=0.005), FeNa </= 0.2% (OR 12.77; 95% CI 3.5 – 46.4; p<0.001), any underlying infection (OR 5.44; 95% CI 2.4 – 11.86; p=0.03) and exposure to nephrotoxic drugs (OR 4.83; 95% CI 2.21 – 10.54; p <0.001) to be significantly associated with AKI. Male gender, serum albumin ≤ 1.4g/dl, infection and FeNa ≤0.2% revealed good accuracy (AUC of 0.86) in predicting subsequent AKI development Duration of hospital stay was significantly longer in children with AKI [Mean

13.6±4.6 days vs Mean 7±1.8 days, p<0.001] and it increased with increasing severity of AKI. Majority had transient AKI (75%, n=27) and of the 5 (14%) children with AKD, 2 (5.5%) progressed into CKD. One child, with AKI stage III on peritoneal dialysis, succumbed to sepsis in PICU.
Conclusion: In this largest prospective cohort of hospitalized cNS, AKI was found to be a common complication in 18%. We identified risk factors at admission with potential to guide subsequent in hospital management which needs validation in larger multicenter cohorts.

Nephrotic syndrome

P3-534 - Comparative Tacrolimus Treatment of Pediatric Steroid-Resistant Nephrotic Syndrome with and without Detected Mutations. Multi-Center Experience

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Introduction: Nephrotic syndrome (NS) is a very frequent pathology in pediatric nephrology. Treatment of steroid-resistant nephrotic syndrome (SRNS) in our field is based on Cyclophosphamide (CP); in CP-resistant patients, alternative regimens are required. International guidelines recommend calcineurin inhibitors (CI) as the first choice: tacrolimus (TC). It has been found that TC is more potent both in vivo and in vitro. Our center uses TC as the first choice in CP-resistant patients,in all cases clinical exome sequencing for SRNS mutations is performed. We present the outcome of 15 patients treated with TC between 2019 and 2022.
Objectives: To assess in our patient cohort complete,partial remission and no remission rate; relapse rate after treatment completion; and adverse events.
To associate such variables with the presence or absence of mutations with clinical significance and uncertain clinical significance.
To associate remission rate with the presence or absence of variants and histological pattern.
Description: We report our center's medium-term follow-up results of SRNS patients treated with TC. Comparative response is assessed in two groups: with or without detected mutation. All patients underwent renal biopsy and clinical exome genetic testing. 2019 IPNA guidelines was used. Fifteen patients were eligible. Histopathological findings: focal and segmental glomerulosclerosis; diffuse mesangial proliferation with IgM deposits and minimal changes. Pathogenic variants were detected in 2 patients; there was uncertain clinical significance in 6; and no mutations were found in 7.The variables analyzed were: average follow-up time; response median; complete and partial remission; no remission; relapse rate after treatment; presence of adverse events.
Conclusion: TC proved to be a safe and effective drug to treat pediatric SRNS. In our group of patients, the remission rate and presence of serious adverse events was similar to the figures reported in the literature. We also deem proteinuria control by non-immune mechanisms to be beneficial in patients without complete remission.

Nephrotic syndrome

P3-535 - Immunoglobulin immunoadsorptions are efficient in the treatment of multidrug-resistant idiopathic nephrotic syndrome in pediatric patients

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Background: Idiopathic nephrotic syndrome is mostly a chronic disease, which can lead to end-stage renal disease in case of corticoresistance and multidrug-resistance.
The aim of this study was to analyze the evolution of pediatric patients with multidrug-resistant nephrotic syndrome treated by immunoglobulin immunoadsorptions (IA) associated with intravenous immunoglobulins (IvIg).
Methods: In this multicentric retrospective study, 30 patients with calcineurin inhibitors (CNI)-resistant steroid-resistant nephrotic syndrome (SRNS) or multidrug-resistant SRNS (with negative genetics) were treated with an association of IA and IvIg, followed by B cell depletion when in remission. The primary outcome was the remission of proteinuria (uPCR<0,05 g/mmol).
Results: A remission was obtained in 23 patients (22 complete remission, 1 partial remission). 16 patients responded during the first cycle of treatment (10 daily sessions of IA), 6 after a more prolonged treatment (up to 3 months), and one after 3 months of treatment. Anti-CD20 monoclonal antibodies were administered to induce B cell depletion in patients in remission. 17 patients relapsed post IA, and 8 developed a dependency to IA to remain in remission (more than 3 months of IA). Only 7 patients did not respond to IA therapy and they progressed towards end-stage renal disease.
On long-term follow-up (mean 49 months), 17 patients were in complete remission (10 of them with no immunosuppressive therapies), and 4 in partial remission (3 of them with no immunosuppressive therapies), all of them with CKD stage 1 or 2.
Conclusions: IA therapy is effective in inducing remission in children with CNI-resistant SRNS or multidrug-resistant SRNS. However, 74% of the patients relapse despite B cell depletion and a significant number of these patients become dependent on IA to maintain remission (35%). Newer treatment strategies are needed to maintain remission and allow IA discontinuation in these children.

Nephrotic syndrome

P3-536 - Daratumumab enables sustained remission after Immunoadsorption in Refractory Multidrug Resistant Nephrotic Syndrome.

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Background: Multidrug Resistant NS (MRNS) is a dramatically challenging condition that may lead to end-stage renal disease and post-transplant recurrence. Immunoadsorption of Immunoglobulins (IA) has been reported safe and efficient to induce remission, however most patients relapse after discontinuation. Long-lived plasma-cells may be responsible for refractory NS. We report the use of Daratumumab(DARA), an antiCD38 monoclonal antibody targeting plasma-cells, in IA-dependent MRNS.
Methods: In this retrospective multicenter study, we included children with MRNS that reached complete remission after IA, but relapsed when lowering frequency of sessions despite B-cell depletion. We report on a further attempt of IA withdrawal adding 4 weekly infusions of DARA (1000mg/1.73m$^{2)}$.
Results: Four boys and 2 girls were included. Median age at diagnosis was 6.1 years (range 5.5-7.9). Renal biopsy showed FSGS in 3 patients and MCD in 3. All had negative genetic testing. All were resistant to ciclosporine and/or tacrolimus, 4 also received MMF and 3 rituximab (RTX). Median time between INS diagnosis and IA initiation was 1 year (0.5-5.6). All patients achieved complete remission after IA but relapsed after a first discontinuation attempt, despite B-cell depletion with RTX(n=3) or Obinutuzumab (OBI) (n=3). Complete remission was again obtained with intensive IA in all but one with partial remission. All patients received a new infusion of OBI followed by 4 infusions of DARA. Complete remission was sustained in all patients enabling IA withdrawal. Proteinuria relapsed in 4/6 (RPC 0.05-0.10g/mmol) and was successfully treated with either a single reinjection of DARA (n=2) or combined to OBI and/or IA. All patients were in complete remission at 7 months (1.5-17.5) following IA discontinuation.
Conclusion: The association of plasma-cell depletion with daratumumab to B-cell depletion allowed IA discontinuation in all patients. Further studies are needed to confirm the efficacy of daratumumab in children with MRNS and better define its place in the treatment strategy.

Nephrotic syndrome

P3-537 - Epidemiology of childhood INS during COVID-19 Pandemic and lockdowns in France and Netherlands.

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Introduction: The etiology of idiopathic nephrotic syndrome (INS) remains partially unknown. Viral infections have been associated to INS onset. We hypothesised that both SARS-CoV-2 infection and lockdown measures could influence INS incidence. The aim of this study was to describe the incidence of childhood INS before and during the COVID-19 pandemic in two European regions.
Material and methods: A survey was sent to pediatric departments in Paris area (France) and the Netherlands. Children with INS onset between 2017 and 2020 in Paris and 2018-2021 in the Netherlands were included. We estimated incidences using census data of each region. Incidences were compared to previous cohorts (Paris: 2008-2013; Netherlands 2006-2009) using two proportion Z-tests.
Results: A total of 248 and 118 cases of INS were reported in Paris area and the Netherlands, respectively, corresponding to an annual incidence of 2.61 and 1.04. Boys were more frequently affected. Incidence was not significantly different before and during the pandemic nor compared to earlier cohorts. During lockdowns, incidence was lower in both countries: 0.76 vs 2.71 (p=0.02) in Paris and 0.42 vs 1.09 (p=0.001) in the Netherlands. During peaks of hospital admissions for COVID-19, no case of INS was reported in Paris nor the Netherlands.
Discussion: Over the last decade, incidence of childhood INS was stable in both European areas. However, during lockdowns, incidence of INS was significantly lower. Interestingly, incidences of other respiratory viral infections were also reduced. Together, these results argue again for a link between INS onset and viral infections, while COVID-19 does not appear to be a significative trigger for INS onset in children.

Nephrotic syndrome

P3-538 - Study on the relationship between nephrotic syndrome and atopic diseases in childhood

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Objective: The present study aimed to explore the relationship between nephrotic syndrome and atopic diseases in childhood.
Methods: From 2018 to 2019, 234 children with first-onset PNS were selected for observation and long-term follow-up. Children with low-dose steroid-dependent PNS and elevated IgE were randomly divided into a low-dose steroid only group and desloratadine combined with a low-dose steroid group. For children with steroid-dependent short stature who required immunosuppressive therapy, renal pathology was conducted after negative conversion of the urine protein. For children with a diagnosis of MCD, the extent of podocyte foot process effacement was observed.
Results: The levels of IL-2, IL-4, IL-10, and TNF-α were significantly higher in children with first-onset PNS compared with healthy children. Of the 234 cases with PNS, there were 143 cases (61.11%) with concomitant atopic diseases. Recurrence due to allergy-related factors was greater than that due to infection-related factors, and the rate of recurrence in spring and autumn was higher than that in winter and summer. The total IgE and bradykinin serum levels were significantly higher in children with first-onset PNS and recurrent PNS compared with those in remission. The level of histamine in children with first-onset PNS was higher than that in children with remission (P<0.05). There was a significant increase in eGFR, a significant decrease in serum IgE, and a reduction in the recurrence rate after treatment of desloratadine treatment group (P<0.05). There was no significant correlation between the proteinuria quantification and the extent of foot process effacement.
Conclusion: There existed a high co-morbidity with AD in children with PNS. Desloratadine might enhance the GFR,improve renal function and reduce relapse. The injury to the filtration barrier in MCD might not only be correlated with podocyte lesions but also with some serum permeability factors. Serum IgE, histamine, and bradykinin might be the plasma permeability factors in children with PNS.

Nephrotic syndrome

P3-539 - Rituximab Therapy in Adolescents with Steroid Resistant Nephrotic Syndrome: Case Series

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Background: Rituximab (RTX) as an immunomodulator is one of the standard treatment choices in steroid-resistant nephrotic syndrome (SRNS). However, the off-label indication for SRNS and high cost made RTX highly inaccessible in most developing countries. The aim of this study is to share our experience of RTX treatment in adolescents with SRNS.
Cases: Two female adolescents underwent RTX therapy for SRNS. We performed infection screening for virus and tuberculosis, also lymphocytes subset examination before the treatment. The dose of treatment was 375/$m^2$of body surface area.
Case 1, a 13-years-old girl with focal segmental glomerulosclerosis underwent two sequences of RTX therapy. She was diagnosed as SRNS 10 years before and already received steroid treatment, cyclophosphamide (CPA) pulses, cyclosporine (CSA), and mycophenolate acid (MPA) with adequate doses, hence the remission had never been achieved. Rituximab was given after an episode of AKI stage 3 that put her on hemodialysis for a month. After two sequences of RTX with 8 weeks apart, we continued low-dose of oral steroid, CSA, and MPA. Urine protein creatinine ratio decreased from 12.2 mg/mg to 0.8 mg/mg within 1 year with no side effects. The level of CD19+ was suppressed after 14 days of therapy.
Case 2, a 17-years-old girl with partial sclerosis and crescent underwent one sequence of RTX therapy. She was diagnosed with SRNS four years before and already received combinations of immunosuppressants with unsatisfying results. Seven days after RTX administration, she developed varicella-zoster virus infection in the right hemifacial area involving ophthalmic region. Fortunately, Ramsay Hunt Syndrome was not found. CD19+ suppression was seen 10 days after therapy. However, nephrotic range proteinuria was still present after discharge.
Conclusion: Rituximab induced CD 19+ suppression in adolescents with SRNS. Benefits for treatment should also be followed by close monitoring for side effects, especially infection.

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P3-540 - Biopsy proven primary FSGS in Children- Looking in to the disease status

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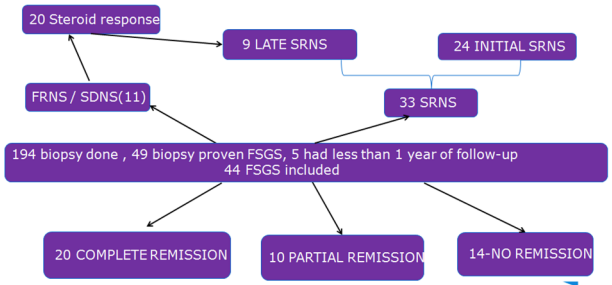
Introduction: Focal segmental glomerulosclerosis (FSGS) is the major cause of steroid resistant nephrotic syndrome leading to end-stage renal disease (ESRD). In early stages it can be indistinguishable from minimal change disease.The clinical course and prognosis of FSGS is heterogeneous in children. FSGS is primarily a histological diagnosis. In India only few studies has been done in children with FSGS.

Primary objective was to assess the risk of ESRD in children with primary FSGS and impact of remission status on diseases progression. Secondary objective of looking in to Demographical profile, treatment response and progression to ESRD was also studied.

Study design: Retrospective observational study with 10 yrs follow up .We had total 194 biopsied children aged between 3 months to 18yrs. Biopsy proven primary FSGS was 44/194. Baseline characters like age,gender, serum albumin,serum creatinine, serum cholesterol,spot urine PCR and hypertension at onset was studied. Histopathological variation was analysed along with treatment characteristrics and side effects.We observed no remission in 32%, complete remission 45% and partial remission in 23%.Prognostic indicators of outcome was analysed.



Predictors		No-ESRD	ESRD	P value
Age at onset	<3y	30(68%)	5(11.3%)	0.19
	>3 y	6(13.6%)	3(6.8%)	
Gender	Male	17(38.6%)	6(13.6%)	0.15
	Female	19(43.1%)	2(45%)	
Histological variant	NOS	30(68%)	8(18.1%)	0.27
	Perihilar	4(9%)	0	
	Tip	2(4.5%)	0	

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P3-542 - Serum magnesium levels and Fractional excretion (FE) of magnesium: a comparison in SSNS and SRNS children

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Background: Utility of FE of magnesium in identifying patients with calcineurin toxicity and tubulointerstitial damage amongst patients with nephrotic syndrome especially SRNS as a non- invasive marker has not been explored previously.
Aims & Objectives: The primary objective of the study was to estimate FE of magnesium and serum magnesium levels in children and adolescents (2-18years) with nephrotic syndrome (both SSNS and SRNS), currently in complete or partial remission.
Methods: This cross-sectional study is ongoing from July 2021-May 22 (n=65); children with CKD stage3 or more, receiving drugs like diuretics, aminoglycosides, proton pump inhibitors, secondary and congenital nephrotic syndrome were excluded. Clinical details were elicited and examination was done. Remission was confirmed with biochemical investigations and serum magnesium levels were estimated. Estimation of urinary magnesium and creatinine was done on a freshly voided urine sample using Vitros 5600 integrated auto analyzer machine with a photometric kit .
Results: 40 (19M: 21F) children (20 SSNS & 20 SRNS) with median age (IQR) 10 years (10;13) have been enrolled till date. The median (IQR) value of serum magnesium was 1.78 (1.7; 2.02) mg/dL and FE of magnesium was 1.56 (0.91;2.29) %. Hypomagnesemia was seen in 60% of children with SRNS and 45% of children with SSNS (P= 0.049).

Increased in FE (>2.2%) of magnesium was seen in 30% of children with SRNS and 20% of children with SSNS (P=0.046).
Conclusion: The prevalence of Hypomagnesemia (60%) and fractional excretion of magnesium (30%) was high in patients with SRNS on CNIs as compared to SSNS disease

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P3-544 - The Role of Short Couse of Daily Prednisolone in Reducing the Frequency of Relapse During Vital Upper Respiratory Tract Infection

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Viral upper respiratory tract infection causes relapse (vURTI) in Nephrotic syndrome (NS). Literature reveals that a short course of daily prednisolone therapy may reduce relapse frequency in patients with steroid-sensitive NS (SSNS). A double blind study aims to evaluate the effectiveness of a short course of daily prednisolone therapy during a vURTI in reducing relapse frequency in children with frequently relapsing NS (FRNS). This trial was carried out in the Department of Pediatric Nephrology, Dhaka Shishu Hospital from March 2018 to October 2019. A total of 68 patients with FRNS who are not receiving steroid or steroid-sparing agents at that time were included. Patients were allocated in Group A and Group B by block randomization. During each episode of vURTI patients randomized in Group A intervene with prednisolone at a dose of 0.5mg/kg for 7 days and Group B with placebo at the same dose and duration. This intervention was repeated for every vURTI during the 9 months follow-up period. Patients were observed for up to 10 days for vURTI associated relapse developing or not. All patients were followed up 3 monthly for 9 months to see the frequency of infections, vURTI associated relapses, total relapses, cumulative dose of prednisolone, and side effects of steroids between the groups. After excluding, 48 patients were examined. Mean vURTI associated relapses were 0.64±0.70 in Group A (prednisolone) and 1.04± 0.56 in Group B (placebo). A significantly ($p<0.05$) reduced rate of relapse had been observed in FRNS children who were treated with a low dose of steroid during the onset of vURTI. Mean total relapse had also been reduced in Group A (prednisolone) in comparison to GroupxiB (placebo) (1.28±0.74. vs 1.83±0.94, $p<0.05$). Administration of a short course of daily prednisolone therapy during a vURTI is effective in reducing relapse in children with FRNS.
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P3-545 - Proteinuria in Asymptomatic Siblings of Children with Steroid Resistant Nephrotic Syndrome: A Screening Using Urinary Dipstick

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Abstract:

Objective: To screen asymptomatic siblings of steroid-resistant nephrotic syndrome patients for proteinuria using the urinary dipstick method to determine the involvement of siblings in the familial and likely genetic cause of the steroid-resistant nephrotic syndrome.
Methods: This cross-sectional study was performed at the outpatient department of Sindh Institute of Urology and Transplantation (SIUT) from January to March 2021.
Results: Out of 104 patients with steroid-resistant nephrotic syndrome, siblings of 66 patients were enrolled. Mean age of primary patients with steroid resistant nephrotic syndrome was 8.7±4.34 years. Most common histopathological diagnosis was focal segmental glomerulosclerosis in 25 (37.9%) children followed by minimal change disease in 17(25.8%) of them. The majority, 48 (72.7%) patients were on immunosuppressive treatment, while 4 (6.1%) had progressed to chronic kidney disease (CKD). A total of 178 siblings were recruited in the study. There were 99(55.6%) boys and 79(44.4%) girls. Their mean age was 10.67±6.2 years. Consanguinity was high in our study population i.e. 56(84%) families. Positive proteinuria on dipstick was detected in only 5(7.5%) enrolled SRNS families. One family refused further testing. Two of the five affected siblings had nephrotic range proteinuria. Renal biopsy of one of them showed membranous nephropathy while the second showed mesangiocapillary glomerulonephritis. Both had normal renal functions.

Table 3: Details of five siblings with dipstick positive proteinuria

S. No	Age	Dipstick*		Spot PCR mg/mg	24 hours urinary protein (mg)	Renal biopsy	S. Alb (mg/dL)	S.Cr (mg/dl)
		Proteinuria	Hematuria					
1	A (12 y)	+1	Nil	1.1	480		4.23	0.3
2	B (5 y)	+2	+3	12.1	1820	MN	3.2	0.16
3	C (6 y)	+3	Nil	5.8	1310	MCGN	2.7	0.17
4	D (11 y)	+1	Nil	0.07	NA			
5	E (27 y)	+2	+1	Drop out	480			

MN: Membranous Nephropathy **MCGN:** Mesangiocapillary Glomerulonephritis

Conclusion: The frequency of proteinuria in asymptomatic siblings of children with steroid-resistant syndrome is low in our population despite a high prevalence of consanguineous marriages. Hence, familial involvement of nephrotic syndrome is low and further genetic testing for monogenic causes is required in steroid-resistant nephrotic syndrome cases.

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P3-546 - Knowledge, Attitude and Practices of Parents Regarding Home Management of Nephrotic Syndrome.

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Introduction: Nephrotic syndrome is a pathological entity characterized by massive proteinuria, hypoalbuminemia, hypercholesterolemia and generalized oedema.
Materials and Methods: This aim of this cross sectional comparative study was to assess knowledge, attitude and practices of parents regarding home management of nephrotic syndrome and was carried out in the Department of Paediatric Nephrology, Cumilla Medical College Hospital, Cumilla conducted from April 2019 to October 2019. Study population were parents having children with nephrotic syndrome age

ranging from 1-12 years. A total of 160 parent having children with nephrotic syndrome were included in this study. Knowledge, attitude and practices of parents regarding the home management in control (n=80) and case (n=80) were recorded.
Results: Mean age was almost similar in both groups (6.49 ± 2.67 years vs 6.43 ± 3.06 years). Male to female ratio were respectively 1.7:1 and 1.9:1 in both groups. Mean score of knowledge about signs and symptoms was 6.41 ± 1.68 in cases which was significantly ($p<0.001$) higher than controls (2.88 ± 0.96). Mean score of practices of home management were 6.35 ± 2.20 in cases and 2.45 ± 1.09 in controls, there was significant difference between cases and controls ($p<0.001$) Attitude regarding home management of nephrotic syndrome was found significantly ($p<0.001$) higher in case than that of control (7.80 ± 1.10 vs 2.81 ± 0.85). There was significant positive correlation of knowledge of home management of nephrotic syndrome with practice ($r = 0.979$ and $p = <0.001$) of home management of nephrotic syndrome. The more the knowledge the more the home management practice.
Conclusion: Practices of home management of nephrotic syndrome are related to knowledge and attitude.

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P3-547 - Determination of frequency of Vitamin A deficiency and its association with relapses among children with nephrotic syndrome

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Vitamin A deficiency is quit prevalent in developing world with a prevalence of 190 million preschool- age children. Vitamin A deficient children as susceptible to develop respiratory and other infections and through activation of Toll like receptors can activate relapse.
Objectives of this study to find frequency of Vitamin A deficiency in children presenting with Nephrotic syndrome diagnosed for 6 months and to determine the association of vitamin A deficiency with relapses in children with Nephrotic syndrome. This was analytical cross sectional study of 150 children with steroid sensitive nephrotic syndrome having age range of 5 to 12 years.
In our study mean age of 8.11±2.75 years and mean duration of nephrotic syndrome was 12.07±3.8 months. 56.7% females and 43.3% male children. 48% were steroid dependent nephrotic syndrome, 18% infrequent relapse and 34% were frequent relapse children Mean vitamin A level was 213±126mg/dl. 16% children vitamin A deficient. More than 2 relapses were present in 37.5% children with vitamin A deficiency and less than 2 relapses in 11.9% in children without vitamin A deficiency, p-value 0.002. Relapses are significantly common in vitamin A deficient cases with duration of 6 to 12 months than those having normal vitamin levels. Relapses are significant in children with Vitamin A deficiency SD type of nephrotic syndrome. A logistic regression was performed to ascertain the effects of age, gender, duration of nephrotic syndrome and vitamin A deficiency in relapses of nephrotic syndrome from 0-2 relapses or more than 2 relapses. The logistic regression model was statistically significant with vitamin A deficiency (p-value: 0.001). Vitamin A deficient cases were 5.7 times more likely to exhibit relapses than normal vitamin A patients.
Conclusion: Vitamin A deficiency is significantly associated with recurrent relapses.

Nephrotic syndrome

P3-548 - The association between hypogammaglobulinemia severity and infection risk in rituximab-treated patients with childhood-onset idiopathic nephrotic syndrome

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Background: Hypogammaglobulinemia is a major adverse event after rituximab treatment. However, the association between rituximab-induced hypogammaglobulinemia and infection frequency is unknown.
Methods: This was a single-center, retrospective, observational study. Patients who received rituximab for complicated nephrotic syndrome between February 2006 and October 2020 were enrolled. Infections requiring antibacterial or antiviral agents or hospitalization were identified, and the characteristics of infections were compared according to infection type. The association between immunoglobulin G (IgG) level and infection frequency was estimated using patient-years analysis.
Results: One-hundred forty patients were enrolled. Fifty infection events were detected in 36 patients, 45 infection events in 32 patients required hospitalization, and 1 severe infection event required intensive care unit admission. In eight patients who developed severe hypogammaglobulinemia (serum IgG level < 200 mg/dL) for more than one year after rituximab treatment, eight infections occurred in six patients, six of these infections were not occurred during period of severe hypogammaglobulinemia. Febrile neutropenia accounted for 54.2% (13/24) of all infections among the patients with hypogammaglobulinemia. The incidence of infections was 0.028, 0.071, and 0.096 patient-years in patients with normal serum IgG levels and those with mild and severe hypogammaglobulinemia, respectively. Immunoglobulin replacement therapy was not administered in any patients except for the treatment of infection.
Conclusions: Our results showed a weak association between hypogammaglobulinemia severity and infection rate. However, the frequency of infection was relatively low even in patients with severe hypogammaglobulinemia, suggesting that, immunoglobulin replacement therapy may not be necessary for rituximab-treated patients with severe hypogammaglobulinemia.

Nephrotic syndrome

P3-550 - Steroid-resistant nephrotic syndrome (NS) after allogeneic hematopoietic stem cell transplantation (HSCT) in a girl with acute myeloid leukemia (AML)

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Introduction: NS is very unusual in pediatric patients treated with HSCT. Graft versus host disease (GvHD), thrombotic microangiopathy and kinase inhibitors toxicity are possible etiopathogenic factors reported. Modification of post-HSCT therapy and kidney biopsy provide some therapeutic clues but no guidelines are available. The aim of the study is to present 12-year-old girl with steroid-resistant NS occurred 6 months after HSCT.

Case report: At the age of 11yr the girl was diagnosed with AML type M2 with mutations in FLT3 and WT1genes (exon 6 c.1092_1093insTACG in the latter). After achieving the remission and conditioning with treosulfan, fludarabine and thiotepa, she underwent HSCT from 10/10 HLA matched brother. Cyclosporine A (CsA) had been used as GvHD prophylaxis for 6 months and sorafenib (an oral multikinase inhibitor) was introduced 2 months after HSCT. Immediately after withdrawal of CsA for high-risk leukemia the girl developed NS. Standard steroid treatment (oral prednisone 60mg/m^2/day) was applied with no effect and a decrease in glomerular filtration appeared (eGFR - 30 ml/min/1,73m^2). Intensification of the steroid therapy (iv methylprednisolone 10mg/kg b.w./every other day, 4 doses) brought normalization of renal function but no remission of proteinuria. Sorafenib was discontinued due to its possible nephrotoxicity and kidney biopsy was performed. The histopathological picture showed an early stage of FSGS (tip lesion variant) with neither glomerular deposits nor any interstitial changes. Three weeks after reintroduction of CsA complete remission was achieved. Return to sorafenib maintenance therapy didn't evoke any side effects. No signs of leukemia relapse were found during a year of follow up after HSCT.
Conclusions: In presented case all known causes of NS after HSCT were excluded. The coincidence of AML, HSCT and NS might be accidental. Nevertheless, the role of WT1 mutation, which is common phenomenon in AML, not previously related to NS in these patients, needs further evaluation.

Nephrotic syndrome

P3-551 - Risk Factors for Chronic Calcineurin Inhibitor Nephrotoxicity among Children with Primary Nephrotic Syndrome Undergoing Long-term CNI Treatment

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Introduction: To determine the effectiveness of calcineurin inhibitors (CNI) and identify the risk factors for chronic CNI nephrotoxicity in children with primary nephrotic syndrome (PNS).
Material & Methods: Characteristics and kidney biopsies of PNS patients treated with cyclosporine (CsA) or tacrolimus (TAC) between Jan 1, 2003, and Dec 31, 2019 were retrospectively reviewed.
Results: Among the 80 patients who received CNI treatment for more than six months, 96 kidney biopsies were performed. Chronic CNI nephrotoxicity (striped interstitial fibrosis with tubular atrophy) was observed in 17.7% (17/96) of kidney biopsies. Our data showed that risk factors for CNI nephrotoxicity in childhood PNS included starting CNI treatment at school-age, persistent nephrotic-range proteinuria for more than 30 days during CNI treatment and CNI resistance (persistent complicated PNS during CNI treatment or resistance to CNI after six months of SRNS therapy). Multivariate analysis revealed that starting CNI treatment during school-age and CNI resistance were independent risk factors for chronic CNI nephrotoxicity. The risks of nephrotoxicity in CsA group and TAC group were similar.
Conclusion: Children with CNI resistance were susceptible to chronic CNI nephrotoxicity. The timing of initiating CNI treatment should be considered carefully, especially during the school-age period.

Nephrotic syndrome

P3-552 - Urinary erythropoietin levels in Nephrotic Syndrome children with Anemia"-a cross sectional study

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Background: Anemia is one of the many complications seen in persistent Nephrotic Syndrome children. In addition to albumin, there is also excessive urinary losses of iron, transferrin, erythropoietin, etc. leading to a deficiency of substrate necessary for effective erythropoiesis. The aim of this study is to estimate urinary levels of Erythropoietin that can be potential cause of anemia in Nephrotic Syndrome.
Settings and Design: It is a cross-sectional study carried out in patients who had Nephrotic Syndrome presented to Pediatric department of Dr Prabhakar Kore Hospital Belagavi, Karnataka, India. All the Nephrotic Syndrome children aged 1 to 18years of age attending outpatient services were screened for Hemoglobin levels and Anemic children were enrolled. Routine investigations with iron studies, Urine, and clinical data were collected from Anemic patients. Measurements of Urinary Erythropoietin were performed with LEGEND MAX™ Human EPO ELISA Kit in Basic Science Research Centre JNMC Belgaum.
Results: Total of 46patients were enrolled according to criteria. Urinary Erythropoietin were significantly higher in Nephrotic Children with Anemia. Among 46 children evaluated (30 [65%] were male and 16[35%] were female) with mean urinary Erythropoietin levels found to be 8.2mIU/ml. Out of 46patients 20-patients underwent biopsy {MCD(9)-mean 12mIU/ml and FSGS(11)-mean 13mIU/ml}.Infantile nephrotic syndrome cases(8%) had higher significant levels-mean-16.2mIU/ml, with steroid dependent cases(69%)-mean-9mIU/ml, steroid resistant cases(13%)-mean-3.79mIU/ml. Urinary Erythropoietin levels were also significantly higher among Frequent relapsers(mean-11mIU/ml) compared to Infrequent relapsers(mean-7mIU/ml).
Conclusions: Urinary loses of erythropoietin were significantly higher in All Anemic Nephrotic Syndrome Children making it a possible cause of anemia along with Iron Deficiency Anemia. Higher significant levels were found in Frequent Relapsing Nephrotic Syndrome and also in Infantile Nephrotic Syndrome.
KEY-WORDS: ANEMIA, NEPHROTIC SYNDROME, Urinary ERYTHROPOIETIN LEVELS

Nephrotic syndrome

P3-553 - Glucocorticoid- and Pioglitazone- Induced Proteinuria Reduction in Experimental Nephrotic Syndrome Both Correlate with Glomerular Extracellular Matrix Remodeling

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Background: Idiopathic Nephrotic Syndrome (INS) is a common glomerular disease, although the molecular cause remains unknown in most children. While glucocorticoids (GC) are the primary treatment, the anti-diabetic PPARg agonist pioglitazone (Pio) also reduces proteinuria in INS and directly protects podocytes from injury. Since both drugs reduce proteinuria, we hypothesized that their similar proteinuria reduction effects result from overlapping gene transcriptional patterns.
Methods: We compared glomerular transcriptomes from rats with PAN-induced NS to those also treated with GC (methylprednisolone) vs. Pio using unsupervised clustering, Ingenuity Pathway Analyses, and web-based bioinformatic platforms.
Results: We identified 29 commonly regulated genes-of-interest, which were primarily involved in extracellular matrix (ECM) remodeling, as well as altered lipid metabolism, DNA-binding, and cytoskeletal organization. These rat genes-of-interest were then compared to those from humans with FSGS in the Nephroseq database, which revealed 12 genes with similar patterns, including upregulation of ECM-regulating genes. We also used previously reported single-cell glomerular transcriptome profiles to deconvolute three glomerular cell lineages (podocytes, mesangial cells, and endothelial cells) from our whole-transcriptome data and compared the gene dysregulation within each glomerular cell type in the PAN+GC vs. PAN+Pio groups. This revealed that most PAN-induced gene dysregulation, as well as GC- and Pio-induced ameliorations, occurred primarily within podocytes, with lesser changes in mesangial cells, and no significant changes in endothelial cells. Finally, we used cultured podocytes and mesangial cells for *in vitro* validation studies of selected genes-of-interest in PAN-induced injury, which highlighted potential roles for Galectin-3 (*LGALS3)* in podocytes and matrix metalloproteinase-2 (*MMP-2*) in mesangial cells in PAN-induced podocyte injury.
Discussion: These studies suggest that preclinical NS models using glomerular transcriptomics may facilitate the identification of novel non-immunosuppressive treatments for INS. Furthermore, this new mechanistic evidence suggests that targeting glomerular ECM dysregulation may enable a future non-immunosuppressive approach for proteinuria reduction in INS.

Nephrotic syndrome

P3-554 - Genetic spectrum of childhood onset steroid resistant nephrotic syndrome in Kazakhstan (preliminary data)

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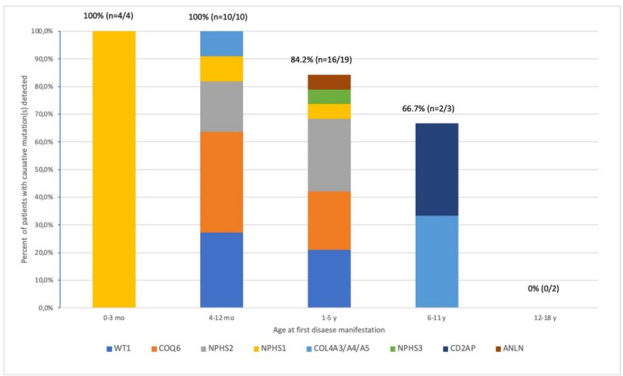
Background and aim of the study. Childhood-onset SRNS has not been studied in Kazakhstan. We aimed to investigate genetic variations of local pediatric patients with SRNS.
Methods: 45 children from birth to 18 years of age with congenital, infantile or steroid-resistant nephrotic syndrome treated at the tertiary referral center between 2016-2021 were selected for the study. 38 (84.5%) of the cohort underwent comprehensive screening using next generation sequencing panels for genes associated with SRNS. Clinical, biochemical, genetic, and histopathologic data were collected both retrospectively and prospectively during the study period. Descriptive data analysis was performed using STATA.
Results: Boys accounted for 73% (n=33), 89% (n=40) were Kazakhs, 11% were Russians. CNS accounted for 9% of all cases, and 82% of the cohort had first disease manifestation before 5 years of age. Kidney biopsy was performed in 26 (57.8%) patients. The most common histopathologic findings were FSGS (53.9%), MCD (11.5%) and MesPGN (11.5%). 33 genetic mutations in 8 genes were detected in 32 (84.2%) of the screened patients. Genetic detection rate was inversely proportional with the age at first disease manifestation (Figure 1). The most common mutations were associated with *COQ6* (n=8, 25%), *NPHS2* (n=7, 21.9%), *WT1* (n=7, 12.9%), *NPHS1* (n=6, 18.8%). All children with COQ6, WT1 and NPHS1 mutations were not related Kazakhs, while 60% (3/5) of not related Russians had mutation in NPHS2.
Conclusions: Male predominance, significantly increased mutation detection rate and *COQ6* mutation frequency were identified when compared with other countries' reports. While single-center cohort and small number of patients were our limitations, we speculate that the evident differences might be partly attributed to the ethnic trait. Further comprehensive genetic screening of a larger multicenter cohort of children in Kazakhstan is warranted to confirm the genetic variation of CNS and pediatric SRNS.

Fig.1 Percentage of children with genetic mutation per gene per age group.



Nephrotic syndrome

P3-555 - Regional variance in childhood nephrotic syndrome outcomes in British Columbia

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Background: In 2013, the British Columbia (BC) Childhood Nephrotic Syndrome (NS) Clinical Pathway was developed to standardize management and improve outcomes of patients with NS. In BC, children access nephrology care at BC Children's Hospital (BCCH) and multiple regional clinics across the province. To ensure equitable access to pathway-recommended care, we compared treatment fidelity and relapse outcomes between BCCH and regional clinics.

Methods: We conducted a retrospective cohort study (2013-2019) of children 1-17 years-old with new-onset NS and at least one year of follow-up. Children with non-minimal change disease, steroid resistance, incomplete induction due to early relapse, or <6 months of pathway exposure were excluded. Clinics were categorized as BCCH or regional (Surrey, Prince George, or Kelowna).
Results: Sixty-nine patients were included, with 52 (75%) at BCCH and 17 (25%) at regional clinics. At BCCH, 37% of patients were female vs. 35% at regional clinics (p=0.93), with a median age of 5.1 years (IQR 6) vs. 4.7 years (IQR 4) (p=0.62). Comparing BCCH and regional clinics, there was no difference in induction prednisone exposure (median 3400, IQR 211 mg/m^2 vs. 3460, IQR 650 mg/m^2, p=0.674) or subsequent clinical course: similar proportions developed frequently relapsing courses (42% vs. 47%, p=0.73) or required steroid-sparing agents (44% vs. 35%, p=0.52). There was no difference in the number of first-year clinic visits (4.2 ± 1.2 vs. 4.0 ± 1.8, p=0.66) or dietitian-reviewed food records (67% vs. 47%, p=0.14) (BCCH vs. regional). However, children at BCCH were more likely to have had a recommended ophthalmology surveillance visit (87% vs. 59%, p=0.01, BCCH vs. regional).
Conclusion: Since the implementation of the BC NS clinical pathway, children with NS receive comparable care and have similar outcomes whether they attend regional or BCCH clinics. Results will be used to inform future pathway improvements.

Nephrotic syndrome

P3-556 - Assessing the accuracy of diagnostic tests to quantify proteinuria in nephrotic children: A cross-sectional study

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ABSTRACT
Objective: To assess the diagnostic accuracy and correlation of 24 hours proteinuria estimation and urine dipstick taking spot urine protein creatinine ratio as gold standard in children with steroid-sensitive nephrotic syndrome.
Study design: Cross-sectional Analytical study
Place and duration of study: Department of Pediatric nephrology, Sindh Institute of Urology and Transplantation from October 2020 to March 2021
Methodology: Proteinuric children were enrolled for quantification of proteinuria by 24-hour urine protein estimation, spot urine protein creatinine ratio and urine dipstick. Sensitivity analysis was performed and receiver operating curves plotted to assess the diagnostic accuracies of 24 hour proteinuria and urine dipstick against spot urinary protein creatinine ratio. Scatter plots compared the correlation of serum albumin and cholesterol with 24-hour urine protein estimation and spot urine protein creatinine ratio.
Results: Forty-two children with median age of 8 years (IQR 6 – 10) were included. Nephrotic range proteinuria was detected in 39 (93%) children with spot ratio, in 16 (38%) cases using 24-hour proteinuria estimation and in 50% with urine dipstick. Twenty- four hour protein estimation showed a sensitivity of 63.4% and urine dipstick a sensitivity of 53.8% in detecting nephrotic range proteinuria when compared to spot ratio with a negative predictive value of 6.3% and 14.3% respectively.
Hypoalbuminemia and cholesterol correlated better with spot ratio as compared to 24-hour proteinuria with r-values 0.0143 and 0.0713 respectively.

Distribution of Clinical and Laboratory parameters of study participants

Clinical & Laboratory Diagnostic Parameters (N=42)		Values N (%)
Serum Albumin (mg/dL)	< or = 2.5 (mg/dL)	30 (71%)
	> 2.5 (mg/dL)	12 (29%)
Serum Cholesterol (mg/dL)	< or = 200 (mg/dL)	6 (14%)
	> 200 (mg/dL)	36 (84%)
Edema	Present	35 (83%)
	Absent	7 (17%)
24 Hour Urinary Protein Volume Collection (ml/kg/hour)	Adequate volume collection (0.5-2 ml/kg/hour)	14 (33%)
	Under collection (< 0.5 ml/kg/hour)	18 (43%)
	Over collection (> 2 ml/kg/hour)	10 (24%)
24 Hour Urinary creatinine (mg/kg/day)	< 10 (mg/kg/day)	22 (52%)
	11 – 20 (mg/kg/day)	15 (36%)
	>20 (mg/kg/day)	5(12%)
24 Hour Proteinuria (gm/m²/day)	=1 gm/m²/day	26 (62%)
	> 1 gm/m²/day	16 (38%)
Spot Urinary Protein Creatinine Ratio (Spot U PCR)	= 2 (gm/gm)	3 (7%)
	> 2 (gm/gm)	39 (93%)
Urinary Dipstick Test	= +3	21 (50%)
	= +3	21 (50%)

Conclusion: Twenty-four hour urine protein estimation and dipstick correlate with spot urine protein creatinine ratio in detection of nephrotic proteinuria with no statistical difference in diagnostic accuracy.

Nephrotic syndrome

P3-557 - A pilot study on the effectiveness of Influenza Vaccination to prevent relapse of steroid sensitive nephrotic syndrome in children.

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Objectives: To study the effect of influenza vaccination in children with Steroid Sensitive Nephrotic Syndrome by comparing the frequency of viral Upper Respiratory Tract Infections (URI) and associated relapses from historic controls.
Materials and Methods: Trivalent, inactivated Influenza vaccine (Influvac 2019/2020) was given to children with steroid sensitive nephrotic syndrome in 2019. They were either on low dose steroids or off medications, and were observed for six months with recordings of their relapses and URIs. They were compared with the same number of unvaccinated children from the previous year.
Results: One hundred consecutive children were vaccinated. Five were lost to follow up. Results of 95 children were compared with equal number of unvaccinated children from the previous year. The mean age of the children was 4.7 ± 2.6 years (range 1-15 years). No side effects of vaccination were seen in any patient. There were 17 episodes of URI in 16 (17%) children in the vaccinated group whereas 69 episodes in 59 (62%) children in the unvaccinated. There were 55 episodes of relapses

Table 1: Upper Respiratory Infection (URI) and Relapses in vaccinated versus unvaccinated children

	Vaccinated Children n =95	Non-vaccinated children n = 95	p value
Total URI episodes	17	69	<0.01
Total patients with URI	16	59	<0.01
Recovered (%)	5	26	<0.01
Relapsed (%)	12	43	<0.01
Total relapse episodes	55	79	<0.01
Total Patients with Relapse	44	71	<0.01
Relapse with URI	12 episodes in 11 patients	43 episodes in 43 patients	<0.01
Relapse without URI	43 episodes in 33 patients	36 episodes in 28 patients	0.18

in 44 (46%) in vaccinated children while there were 79 relapses in 71 (75%) in unvaccinated children. Both the number of URI episodes and relapses were significantly reduced in the vaccinated children (p <0.001) as shown in Table 1.

The odds of getting URI and relapse in them was 0.12 (95% CI 0.06-0.24) and 0.29 (95% CI 0.16-0.54) respectively. No difference was seen in number of relapses that were not associated with URI.

Conclusion: There seems to be a significant decrease in all-cause URI and relapses in steroid sensitive nephrotic children who are vaccinated with flu vaccine. Further trials in larger cohorts are required to confirm the beneficial effect of this recommended vaccination.

Keywords: Steroid-sensitive Nephrotic Syndrome, Viral Upper Respiratory Tract Infections, Influenza Vaccine.

Nephrotic syndrome

P3-558 - High Dose Rituximab, Mycophenolic Acid, and Calcineurin Inhibitors Achieve Long-term Remission in Pediatric Refratory Nephrotic Syndrome due to Focal Segmental Glomerulosclerosis: A Report of Two Cases

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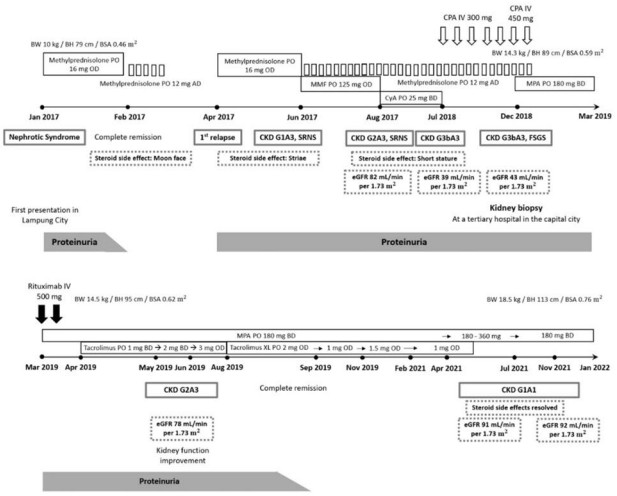
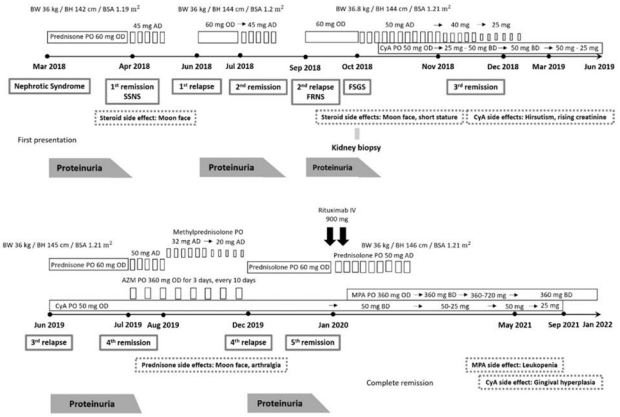
Studies investigating the effect of rituximab in children with nephrotic syndrome (NS) due to focal segmental glomerulosclerosis (FSGS) have reported conflicting results, with some concluding that patients may require additional immunosuppressive therapy to achieve and/or maintain long-term remission. We report successful treatment of pediatric FSGS with high-dose rituximab infusions, followed by maintenance immunosuppression with mycophenolic acid (MPA) and a calcineurin inhibitor (CNI) in one patient with refractory steroid-resistant NS (SRNS), and one with frequently-relapsing NS (FRNS). Case 1 is a patient with refractory SRNS due to FSGS. MPA and tacrolimus induced complete remission within 6 months following high dose rituximab treatment. Remission was maintained for over 2 years, and the patient's kidney function and height also returned to normal ranges within this time. Case 2 is a patient with FRNS due to FSGS, who was treated with rituximab followed by MPA and cyclosporine, which successfully prevented relapses for 18 months. Our case report demonstrates that high dose rituximab and a combination of CNIs and MPA can be effective in achieving complete remission in pediatric refractory SRNS, and sustaining remission in pediatric FSGS with FRNS and SRNS for several years. This treatment regimen has the advantage of eliminating the need for long-term high dose steroid treatments, allowing one patient to achieve normal growth and recover from other adverse steroid effects.

Timeline of Case 1



Timeline of Case 2



Nephrotic syndrome

P3-559 - Congenital nephrotic syndrome of Korea; an experience of last 20 years in a referral hospital

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Background: Congenital nephrotic syndrome (CNS) is a rare disorder, whose major causes are genetic defects in the components of the glomerular filtration barrier. CNS is complicated with severe edema, malnutrition, sepsis and thrombosis. Rarity of this condition also contributes to the difficulties of managing physicians.

Methods: A retrospective, single-center study of children diagnosed as CNS during last two decades.
Results: Thirty-three children (21 males) with CNS had developed earlier than their age of 3 months were included. Their median age at diagnosis was 40 days (ranges 1-180) with presentation of edema (n=21), end-stage kidney disease (ESKD, n=9), or lethargy (n=3). Pathologic findings (n=13) were FSGS (6), MPGN (2), and single cases of MCD, diffuse mesangial sclerosis, immune mediated nephropathy, diffuse proliferative GN, non-specific nephropathy. Causes of secondary cases were secondary to congenital infection (n=2) or severe renovascular hypertension, or capillary leak syndrome. Genetic testing (n=29) revealed mutations of *NPHS1* (14), *WT1* (9), *LAMB2* (1), *PODXL* (1), *CFH* (1), and none (3). For treatment, 11 were treated medically with indomethacin and/or captopril, and nephrectomy was performed to reduce proteinuria (unilateral, n= 3 with *NPHS1*) or to prevent the occurrence of Wilms tumor (bilateral, n= 3 with *WT1* defect). 23 patients reached ESKD at their age of 41.4 ± 64.1 months, and six patients (*NPHS1*(2), *WT1*(1), *PODXL*(1), unknown (2)) expired at a median (range) age of 3.8 (0.3-123) months from uncontrolled infection (n=2), multiorgan failure (n=3), and complication of kidney transplantation (n=1). Three patients (genetic defects unknown) achieved spontaneous remission without relapse.
Conclusions: Most of the CNS were of genetic causes and *NPHS1* was the most common cause in our cohort as well. Presentation with EKD was common with *WT1* defect. Remission was achieved in 9% in whose genetic causes were unknown, and mortality rate of CNS was 18%.

Nephrotic syndrome

P3-562 - Collapsing Focal Segmental Glomerulosclerosis in children: a Colombian case series

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Introduction: Focal Segmental Glomerulosclerosis (FSGS) is a glomerulopathy characterized by podocyte damage and capillary collapse frequently associated to corticosteroid resistance. There are different histologic categories such as the collapsing variant, which is typically associated to acute kidney injury and a poor response to treatment leading to chronic kidney disease (CKD).
Methods: We perform an observational retrospective study describing clinical information from collapsing FSGS patients in the Fundación Hospital de la Misericordia in Bogotá, Colombia between June 2016 and June 2021.
Results: We evaluated 8 patients with a mean age of 12.4 years old, 6 boys. At debut every child had nephrotic syndrome associated to hypertension, mean proteinuria 7.030 mg/24 hours, albumin 2.2 g/dL and GFR 38 ml/min/1.73m2. Two children had a rapidly progressive evolution needing dialysis immediately. The glomerular sclerosis percentage was 42% (41% segmental, 59% global). The immune (ANAS, anti-dsDNA, ANCA and complement) and infectious test (HIV, Hepatitis B and C, CMV, EBV) were negative in every patient. All patients received steroid treatment (75% methylprednisolone bolus), three were treated with cyclosporine, two with cyclophosphamide and another had both. At 218 days of mean follow up, only two children had a possible etiology, one patient with Galloway Mowat syndrome, and another had SARS-CoV-2 infection three months before; two remained with reduced kidney function, one child had a kidney transplant, another died, the remained patients persisted with significant proteinuria and a mean GFR 61,6 ml/min/1.73 m2.
Conclusion: Collapsing FSGS is infrequent in children. It is characterized by a poor response to immunosuppressive treatment and increased risk of progression to CKD. In our series, the results are similar to those seen in the literature, the etiology is idiopathic in most cases and at follow up, kidney function remain reduced with persistent proteinuria.

Nephrotic syndrome

P3-563 - Prevalence of antineutrophil cytoplasmic antibodies in Indian children treated with levamisole for nephrotic syndrome

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Background: Levamisole is a common alternative therapeutic agent used in the management of frequently relapsing/ steroid dependent nephrotic syndrome (NS). Although it is usually considered a safe therapeutic agent, drug-induced anti-neutrophil cytoplasmic antibody (ANCA) positivity and ANCA vasculitis is dreaded complications associated with its use. A recent report mentions ANCA positivity rate of 18% and ANCA vasculitis observed in 3% of children who were treated with levamisole for nephrotic syndrome.
Objective: Identify the prevalence of ANCA vasculitis in nephrotic syndrome in children treated with levamisole.
Methods: Data was collected from the electronic health records regarding children with NS, managed with levamisole therapy from 2015 to October 2021. Definition of NS, remission and relapses were described as per Indian Society of Pediatric Nephrology guidelines 2008. ANCA antibodies were performed using enzyme-linked immunosorbent assay (ELISA) and levels of anti-myeloperoxidase (MPO) and anti-proteinase 3 (PR3) above 20 U/L were considered as positive.
Results: Among 135 children (67% male) treated with levamisole for nephrotic syndrome during the time period, 57 children had at least one ANCA antibody level tested. Six (10.5%) had positive ANCA levels. One child had antiphospholipid syndrome with pancytopenia, hepatosplenomegaly and gangrene of toes, 23 months after starting levamisole therapy, along with ANCA positivity. Levamisole was discontinued and he remains in remission with ANCA antibodies negative six months after discontinuation. Four of these six children had repeat ANCA testing; antibodies were negative in two children and they persisted to be positive in two children, 3-6 months after stopping levamisole. Five children developed transient leucopenia (including one child with severe neutropenia) during therapy; none of these children developed any infectious complications during neutropenia.
Conclusion: ANCA antibody positivity is not uncommon during levamisole therapy; due diligence must be observed by physicians.

Nephrotic syndrome

P3-564 - Precise clinicopathologic findings for application of genetic testing in pediatric kidney transplant recipients with focal segmental glomerulosclerosis/steroid-resistant nephrotic syndrome

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Background: Establishing a molecular genetic diagnosis of focal segmental glomerulosclerosis (FSGS)/steroid-resistant nephrotic syndrome (SRNS) can be useful for predicting post-transplant recurrence. Monogenic causes are reportedly present in approximately 20%–30% of patients with FSGS/SRNS. However, the characteristics of patients who are likely to have a monogenic cause remain to be determined.
Methods: Pediatric recipients with SRNS and/or biopsy-proven FSGS who underwent their first kidney transplantation at our center between 1999 and 2019 were analyzed. Patients with secondary FSGS/SRNS were excluded. The recipients were divided into three groups: familial/syndromic, presumed primary, and undetermined FSGS/SRNS. Patients who met all of the following criteria were categorized as having presumed primary FSGS/SRNS: (i) nephrotic syndrome, (ii) complete or partial remission with initial steroid therapy and/or additional immunosuppressive therapies, and (iii) diffuse foot process effacement on electron microscopy in the native kidney biopsy. All patients underwent genetic testing using next-generation sequencing.
Results: Twenty-four patients from 23 families were analyzed in this study. Pathogenic or likely pathogenic variants in FSGS/SRNS-related genes were identified in four (100%) of four families, zero (0%) of eight families, and 10 (91%) of 11 families with familial/syndromic, presumed primary, and undetermined FSGS/SRNS, respectively. Post-transplant recurrence only occurred in patients with presumed primary FSGS/SRNS.
Conclusions: Our systematic approach based on precise clinicopathological findings including nephrotic syndrome, treatment responses, and diffuse foot process effacement may be useful to differentiate pediatric kidney transplant recipients with FSGS/SRNS who are likely to have a monogenic cause from patients who are not, and to predict post-transplant recurrence.

Nephrotic syndrome

P3-565 - Adrenocortical suppression in children and adolescents with nephrotic syndrome treated with corticosteroids.

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Adrenocortical suppression in children and adolescents with nephrotic syndrome treated with corticosteroids

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Background: Prolonged use of steroids tend to cause adrenocortical suppression; while single morning cortisol levels are used for screening purpose low dose ACTH stimulation is confirmatory.
Aims & Objectives: The primary objective of the study was to determine the prevalence of ACTH suppression in SSNS or SRNS children and adolescents (2-18 years), who were on either low dose alternate day steroids(<1mg/kg/day) or off steroids for atleast 2 months, and currently in partial or complete remission.
Methods: This cross-sectional study is ongoing from Oct 2021-June 2022(n=50). Children with nephrotic syndrome who received daily corticosteroid therapy in any dosages presently or having serious bacterial infections or hospitalised for any reason were excluded. Clinical details were elicited and examination done. Remission was confirmed. Blood investigations with LFT,KFT,Lipid profile,HbA1C,baseline and post-stimulation (with 25 units of ACTH)S. cortisol were estimated to identify adrenocortical suppression. Levels below 18microgram/dL were considered low.
Results: 30(11F;19M) children with median(range)age 10.1(3-17) years have been enrolled(14 SSNS and 16SRNS)till date;Among SSNS 6 were SDNS(43%),5 were FRNS(36%)and 3 were IFRNS(21%).Stunting was noted in 16%(25% of SRNS and 7% of SSNS).The mean baseline S.cortisol value was 6.805mcg/dl. Overall 94% of patients had baseline ACTH suppression(94% of SRNS and 85% of SSNS/SDNS/FRNS). The mean post stimulation S.cortisol value was 16.25 mcg/dl. The prevalence of steroid suppression had decreased to 60% after low dose ACTH(56.25%SRNS ad 64% SSNS).69% of patients (81% of SRNS and 57% of SSNS) had hypertension and 12% of SRNS patients had hyperglycemia and none of SSNS patients have hyperglycemia.
Conclusion: The prevalence of adrenocortical suppression is high among both SSNS and SRNS patients on low dose alternate day steroids.

Nephrotic syndrome

P3-566 - Diffusion and severity of SARS-COV-2 infection among children affected by idiopathic nephrotic syndrome

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Introduction: Since 2020, SARS-CoV-2 caused over 6 million deaths, mostly in adults. Children display a milder course even when affected by chronic kidney diseases or on immunosuppression. Nonetheless, idiopathic nephrotic syndrome (INS) has been advocated as a predictor of worst outcome. We aimed at investigating the diffusion and severity of SARS-CoV-2 infection among children with INS.
Methods: By a phone-based questionnaire, we retrospectively collected information from the beginning of the pandemic to March 31, 2022, regarding the incidence and characteristics of SARS-CoV-2 infections and vaccination status in children (0-18 years) affected by INS and followed by the Pediatric Nephrology Unit of Milan.
Results: A total of 158 patients were enrolled (median age 7 years). 33 were affected by an infrequent relapsing nephrotic syndrome (IRNS), 102 by a steroid-dependent/frequent-relapsing nephrotic syndrome (SDNS, FRNS) and 23 by a steroid-resistant nephrotic syndrome (SRNS). 98/158 were on immunosuppressive therapy. A total of 51/158 (32%) patients with a median age of 9 years reported a previous SARS-CoV-2 infection documented by nasal swab: 7/51 were affected by IRNS, 36/51 by SDNS/FRNS, and 8/51 by SRNS. 21/51 patients had been previously vaccinated for SARS-CoV-2 with at least two doses and 36/51 patients were on immunosuppressive drugs. No hospitalization or deaths were reported. Symptoms were absent in 12/51 patients or mild (fever, rhinitis, cough) in 39/51 patients. In no cases, modifications of the immunosuppressive therapy were required. All SDNS, FRNS and IRNS patients performed urine dipstick during the infection and in 5/43 (11.6%) proteinuria was detected, but only two patients had a clinical relapse requiring steroid therapy. Proteinuria resolved in a median of 7 days.

Conclusion: In this large cohort of children with INS and SARS-CoV-2 infection, symptoms were mild, even on immunosuppressed and SRNS patients. Transient proteinuria was common, but with a low rate of relapses.

Nephrotic syndrome

P3-567 - Efficacy of the levamisole in pediatric patients with idiopathic sensitive nephrotic syndrome frequent relapse or steroids dependent in a single center

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Introduction: Nephrotic syndrome is one of the most frequent glomerular diseases in pediatric population. The aim of the study was to describe the efficacy of levamisole as a corticosteroid-sparing agent in the pediatric population diagnosed with frequent relapsing nephrotic syndrome and corticosteroid- dependent nephrotic syndrome.
Methods: A retrospective cohort study was carried out and included patients younger than 18yr old and older than 1yr at the time of diagnosis of nephrotic syndrome. The definitions of nephrotic syndrome as well as, corticosteroid dependence and relapse were based on the KDIGO criteria.
Results: 30 patients were selected. The average age of onset of the disease was 4yr old with a minimum age of 1yr and a maximum age of 11yr. The dose of corticosteroids used in all patients at the beginning of the episode of nephrotic syndrome was 2mg/kg/day. The most commonly used corticosteroid sparer before using levamisole was cyclophosphamide (26.7%). Of the adverse events found, 86.7% of the patients had no adverse effects related to levamisole, 3.3% had headache, 3.3% neutropenia and 3.3% urticarial reaction. Regarding the performance of biopsy, 70% of the patients did not undergo a biopsy. The most common finding was FSGS (13.3%) followed by minimal injuries (10%) and chronic nephritis (6.7%). Throughout the 1yr assessment, there was no worsening of any hemantimetric index. P value was considered >0.05 for all analyzed variables. For non-normal variables the Wilcoxon test was performed. The rate of reduction of relapses with one year of levamisole use was statistically significant ($p = 0.001$) with an average reduction of 4 episodes for no episode.
Conclusion: The present study demonstrated the effectiveness of levamisole in reducing the number of relapses in the first year of use, with low rates of adverse events, reaffirming its use can be considered as an important corticosteroid-sparing drug.

Nephrotic syndrome

P3-569 - Parental perception of steroid side-effects in children with nephrotic syndrome

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Introduction: The incidence of corticosteroid-related side-effects is well documented. This study aimed to explore parental perceptions of side-effect severity in children with nephrotic syndrome.

Method: An anonymous online survey aimed at parents of children with nephrotic syndrome was disseminated via UK social media accounts of the Nephrotic Syndrome Trust and individual paediatric renal units, and ran for 6 weeks from December 2021. Parents rated 19 standard side-effects according to a severity score (None = 0; Mild = 1; Moderate = 2; Severe = 3). Patient scores were summated without any weighting (maximum score: 57). Parents were asked to rank the 3 most severe side-effects. Individual side-effects were ranked in severity for the whole group.
Results: 78 responses were received. 59% of patients were male. Median side-effect severity score was 14.0 (Interquartile range 10-19). There was no significant difference between males (14.5) and females (15.7) (p=0.48). Scores were higher in those with a disease duration >10 years (20.2), and in those who had experienced >30 relapses (21.3). Children diagnosed after 11 years had lower side-effect scores (9.0). Rapidly changing mood, aggressive behaviour, round face, weight gain and poor sleep were most frequently ranked as the most severe side-effect. Side-effects relating to behaviour were reported to be more severe in boys, and those relating to changes in appearance more severe in girls.
Conclusion: This is the first exploration of parental perception of relative severity of corticosteroid-related side-effects in childhood nephrotic syndrome. Overall perception of side-effects was greater in those with a longer duration of disease or more frequently relapsing course. Behavioural/emotional issues and changes in appearance are perceived as the most severe side-effects, with interesting gender-differences. These results form a starting point for further patient-reported research towards validated corticosteroid side-effect scores for use as outcome measures in clinical trials.

Nephrotic syndrome

P3-570 - NPHS (1/2) Mutation associated Congenital Nephrotic Syndrome – A National Experience.

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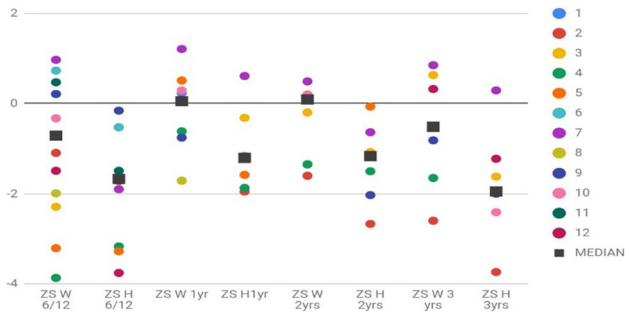
Intro: Expert consensus guidelines have recently been published for the management of Congenital Nephrotic Syndrome (CNS). In this review we outline the management of 12 patients with CNS over a 20year period, that broadly mirror the recommendations outlined in these guidelines.
Methods: A retrospective review was performed of all patients with confirmed NPHS1 or NPHS 2 CNS in the Republic of Ireland between 1998 and 2018. Demographic and outcome data was collected.
Results: 12 patients were included (9 NPHS1 and 3 NPHS2). The median age at presentation was 4.5 weeks. 10 patients were commenced on regular albumin infusions and all 9 NPHS1 patients underwent unilateral nephrectomy, median age 4.5 months. There was a significant reduction in albumin infusion post-surgery ($p < 0.05$). One patient developed a thrombotic complication. Routine thrombo-prophylaxis was otherwise not routinely prescribed. Median weight and height SDS were described. Our group did not show significant change in SDS after 6 months on dialysis. Median age at renal replacement therapy was 18 months for NPHS1 patients.



A Scatter plot representing the Z scores for weight and height of each of the subjects at 6 months, 1 year, 2 years and 3 years of age.
Conclusion: Our centre has adopted a treatment approach over the last 20 years that is broadly in line with recently published guidelines and we have presented patient follow up data having utilized albumin therapy, unilateral nephrectomy and anti-proteinuric medication. There is still much to study with regard to CNS, especially neurocognitive and motor development and the sequelae of dyslipidaemia.

Nephrotic syndrome

P3-571 - Experiences and healthcare priorities of childhood steroid sensitive nephrotic syndrome: perspectives of children and their caregivers

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Background: Childhood steroid sensitive nephrotic syndrome (SSNS) runs a relapsing and remitting course. Children with nephrotic syndrome and their caregivers are reported to have poor quality of life.
Aim: We aimed to explore the experiences and healthcare priorities of children with SSNS and their caregivers.
Methods: We conducted semi-structured interviews with children with SSNS and their caregivers from January to April 2021. We used thematic analysis to analyze the data.
Results: There were 28 participants that comprised of 10 children aged 9 to18 years (6 boys and 4 girls) and 18 caregivers (8 men and 10 women). Three themes that describe participants' experiences were identified: (a) disruption of normalcy, (b) regaining control, and (c) dependable social support system. Four actionable needs and priorities were identified: (a) desire to be heard; (b) understanding the etiology of nephrotic syndrome; (c) alleviating the burden of steroid regimen and (d) enhanced social support availability. Overall, participants described being resilient and adapting their life goals to accommodate SSNS into their lives.
Conclusion: Children with SSNS and their caregivers experience disruptions in their lives as a result of recurrent relapses, side effects of steroid medication and disease uncertainties. Strategies to provide support for children with SSNS and their families should be developed and implemented.

Nephrotic syndrome

P3-572 - Efficacy of rituximab in childhood idiopathic nephrotic syndrome – a systematic review and meta-analysis

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Background: Patients with steroid dependent nephrotic syndrome (SDNS)/frequently relapsing nephrotic syndrome (FRNS) require steroid sparing medications to prevent relapse. These agents rarely induce remission in steroid resistant nephrotic syndrome (SRNS).
Objective: To determine the efficacy and safety of rituximab in childhood idiopathic nephrotic syndrome by synthesizing results from randomized controlled trials.
Method: We searched MEDLINE, EMBASE, Web of Science Core Collection and Cochrane Library from inception to April 13th, 2022 using search terms for nephrotic syndrome and rituximab. The study protocol was registered in PROSPERO (CRD42020216260)**.** Randomized controlled trials were included if they involved children ≤ 18 years with SDNS/FRNS or SRNS and compared rituximab to placebo, or non-corticosteroid immunosuppressives.
Results: We identified 10 studies that included data from 457 children. Six papers compared rituximab with placebo. Only one study compared rituximab to tacrolimus in SDNS/FRNS while 3 studies compared rituximab to standard therapy in SRNS. Risk of bias assessment indicated that 70% of the studies had adequate randomization procedures while 7 studies were open-label trials. In SDNS/FRNS, rituximab significantly reduced the risk of relapse with a pooled risk ratio (RR) of 0.27 (95% CI, 0.11 - 0.70) while in SRNS, rituximab use favored remission with a pooled RR of 1.26 (95% CI, 0.91 - 1.76). The most common adverse effect is infusion reaction reported in 80% of the trials.
Conclusion: Rituximab is effective in preventing relapse in SDNS/FRNS and inducing remission in SRNS. The most common adverse effect associated with rituximab was infusion reaction. We recommend that rituximab should be introduced as a first-line steroid-sparing therapy in childhood idiopathic nephrotic syndrome.

Nephrotic syndrome

P3-573 - Correlation of pathological and genetic findings in childhood nephrotic syndrome

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Background: Although there have been many genetic studies in the nephrotic syndrome, few have had as rigorous an investigation of pathological findings as of the molecular biology, partly because review of material from multiple centres is difficult. Due to the uncertainty about genotype-phenotype correlations we wanted to determine whether there was any correlation between pathological and genetic findings in children with the nephrotic syndrome.
Methods: Any children seen at the Birmingham Children's Hospital with the nephrotic syndrome in whom there had been genetic studies, renal biopsies and/or nephrectomy specimens were included and analysed by a renal pathologist who was unaware of the genetic findings. The pathological findings were grouped into various groups and patterns, before being compared to the genetic findings.
Results: Of 43 children, 15 had mesangial expansion as the main feature, one also with prominent glomerulocystic change, attributed to treatment preceding nephrectomy. Fourteen of these had congenital nephrotic syndrome. In these 15, there were variants in *NPHS1* in ten, in *NPHS2* in one, and in *FAT1* in one. Of 11 children with the classical childhood form of segmental sclerosing disorder, and three with presumed minimal change nephropathy, only one in the former group had a detectable variant, in *CRB2*. In seven with collapsing glomerulopathy, five had variants in *WT1*, *NUP107*, or *PLCE1*. Of six with widespread

segmental sclerosing lesions, one had variants in *TRIM8* and *COL4A3*, and one had an *INF2* variant. One child with overload glomerular changes had a benign variant in *COL4A4*.
Conclusions: We found that variants of specific genes appear associated with typical pathological findings, explained by the limited structural response of the kidney to damage. Conversely pathological findings were not necessarily specific for a single abnormal gene. In our series we found good genotype-phenotype correlation in the nephrotic syndrome compared to reports in previous genetic studies.

Nephrotic syndrome

P3-574 - Cyclosporine increases serum uric acid in children with steroid-resistant nephrotic syndrome due to focal segmental glomerulosclerosis

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Introduction: Immunosuppressive treatment with cyclosporine (CsA) often leads to hyperuricemia in transplant adults' recipients. Data on uric acid kidney handling in children with steroid-resistant nephrotic syndrome (SRNS) due to focal segmental glomerulosclerosis (FSGS) treated with CsA are sparse. This study aimed to identify influence of CsA on kidney handling of uric acid in children with SRNS due to FSGS.
Methods: We conducted retrospective longitudinal study of 24 children (14F/10M) aged 6.5 (IQR: 3.5; 9.5) years at onset of SRNS due to FSGS treated with CsA. Median initial CsA dosage was 4.5 (IQR: 3.9; 5.3) mg/kg/day with blood trough level 122.1 (IQR: 95.5; 134.1) ng/ml. Median time of CsA treatment was 23.0 (17.4; 30.5) months.
Results: We found elevation of uric acid serum level despite stable uric acid tubular reabsorption during treatment with CsA in children with SRNS due to FSGS (Table). The proportion of patients with hyperuricemia increased gradually during CsA therapy: 1/24 (4.2%) before CsA vs. 4/24 (16.7%) at 6 months (p=0.35), 4/22 (18.2%) at 12 months (p=0.18) and 7/19 (36.9%) at 24 months of treatment (p=0.01). All children with hyperuricemia were asymptomatic. The median eGFR decreased during CsA therapy compared with the baseline level (Table). Serum level of uric acid was negatively associated with eGFR during treatment with CsA: at 6 (r=-0.53, p=0.008), 12 (r=-0.46, p=0.037), and 24 months (r=-0.61, p=0.022).
Conclusions: Treatment with CsA led to increased serum level of uric acid in children with SRNS due to FSGS. Hyperuricemia was found in 4.2% patients before treatment with CsA to 36.9% cases at 24 months of the therapy. Monitoring of serum uric acid level during CsA treatment might be useful for early detection of CsA-induced hyperuricemia to prevent worsened kidney outcomes in children with SRNS due to FSGS.

Table. Uric acid kidney handling in children with SRNS due to FSGS treated with CsA

	Before CsA treatment (n=24)	6 months CsA treatment (n=24)	12 months CsA treatment (n=22)	24 months CsA treatment (n=19)	P1-P2	P1-P3	P1-P4
TR uric acid, %*	93 (87.3; 94.8)	93 (91.3; 94)	93 (88; 95)	94 (92; 95)	0.325	0.990	0.131
Serum uric acid, mmol/l*	0.29 (0.21; 0.33)	0.34 (0.28; 0.39)	0.32 (0.26; 0.38)	0.35 (0.25; 0.44)	**0.001**	**0.003**	**0.008**
eGFR, ml/min/1.73 m²*	95.5 (86.9; 111.8)	84.7 (68.6; 93.2)	88.2 (76.8; 107.2)	87.2 (67.8; 101.6)	**0.001**	**0.002**	**0.032**

*Median, IQR

Nephrotic syndrome

P3-575 - The utility of repeat kidney biopsy in children with steroid-resistant nephrotic syndrome due to focal segmental glomerulosclerosis treated with cyclosporine

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Introduction: Kidney biopsy (KB) has been the gold standard for histopathological diagnosis of steroid-resistant nephrotic syndrome (SRNS) in children. However, clinical relevance of the 2nd KB in children with SRNS has been subject to debate. We aimed to evaluate histological characteristics of repeat KB in children with SRNS due to FSGS treated with cyclosporine (CsA).
Methods: We studied 12 children (9F/3M) with SRNS due to FSGS treated with CsA at initial dosage 4.2 (3.7; 5.0) mg/kg/day with blood target trough level of 130.0 (118.6; 143.0) ng/ml after the 1st KB. Acute CsA-induced nephrotoxicity with reversible rising serum creatinine ≥25% from baseline level was found in all patients. Median time between the 1st and 2nd KB was 41.0 (29.0; 45.4) months.
Results: Significant increase in global glomerulosclerosis ≥10% (25% vs. 75%, p=0.039), interstitial fibrosis (33.3% vs. 91.7%, p=0.009) and vascular lesions (0% vs. 41.7%, p=0.037) was observed at repeat KB in comparison with the 1st KB. 5/12 (41.7%) of patients with SRNS due to FSGS had histopathological signs of CsA-induced nephrotoxicity at the 2nd KB. Treatment with CsA at 6 months induced complete and partial remission in 1/12 (8.3%) and 5/12 (41.7%) patients, respectively. Failure to response to CsA was found in 6/12 (50%) individuals. We found no difference in median proteinuria and eGFR at the 1st and 2nd KB: 1.8 (0.2; 2.7) vs. 1.2 (0.2; 4.4) g/d (p=0.770) and 99.0 (91.2; 112.5) vs. 111.5 (89.2; 121.8) ml/min/1.73 m² (p=0.625), respectively.
Conclusions: Significant increase in global glomerulosclerosis, interstitial fibrosis and vascular lesions was found at 2nd KB in children with SRNS due to FSGS treated with CsA. 41.7% of patients had histopathological features of CsA-induced nephrotoxicity at the 2nd KB. Repeat KB in children with SRNS due to FSGS may provide useful information regarding disease progression and avoid repeated treatment with CsA.

Nephrotic syndrome

P3-576 - Diagnostic value of urinary CD80 in typical and atypical nephrotic syndrome

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Background: Along with typical cases, atypical patients presented with gross hematuria, hypertension, sustained serum creatinine elevation, low serum C3 and C4 level. Human T lymphocyte activation antigen CD80 is present on podocytes and its expression is maintained by activity of T-cells. Dysregulation of concentration of CD80 occurs in blood due to T-cell dysfunction. Urinary CD80(uCD80) concentration increases only in patients with typical NS in active state and level remains normal in patients with atypical NS.

Objective: To evaluate uCD80 concentration as a diagnostic marker of typical and atypical NS.
Materials & method: This Cross Sectional study was performed in the Department of Pediatrics & Pediatric Nephrology, Chittagong Medical College Hospital, Bangladesh. Seventy five patients of NS (39 with typical and 36 atypical) were enrolled from January 2020 to July 2021.Urinary CD80 concentration was measured by human sCD80 instant ELISA kit and compared between typical and atypical NS.
Results: Male found predominant and mean age found higher in atypical NS patients. Urinary CD80 concentration found lower in atypical NS patients with hypertension, hematuria, raised serum creatinine and low serum C3 level; found statistically significant, ($p<0.001$). Mean uCD80 concentration in typical NS (671.92 ±328.45) was found significantly higher ($P<0.001$) than atypical NS patients (122.30 ±158.47). Mean uCD80 concentration was 408.11 ± 379.077 ng/g of creatinine. The area under the curve for typical NS was 0.946 for uCD80 concentration (95% CI: 0.899–0.992) ($p<0.001$). Urinary CD80 concentration 114.9 ng/g of creatinine was found most appropriate cut-off value with the sensitivity 92.3% and the specificity 27.8% for the differentiation of typical NS.
Conclusion: Urinary CD80 level found significantly higher in patients with typical NS than atypical NS. Along with the other diagnostic criteria, uCD80 may be used as a non-invasive biomarker to differentiate typical and atypical NS.

Nephrotic syndrome

P3-577 - Evaluation of antibodies levels against hepatitis B and rubella virus in children and adolescents with idiopathic nephrotic syndrome

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Objective: To evaluate the levels of antibodies against hepatitis b virus and rubella in children and adolescents with idiopathic nephrotic syndrome and to determine the factors associated with the alteration of these levels.
Methods: A retrospective study of 63 patients with idiopathic nephrotic syndrome previously vaccinated against hepatitis b and rubella virus were made. The information was obtained from the database.
Results: HBs antibody values < 10mIU/ml were found in 83.6% (51/61) and IgG values for rubella < 10IU/ml in 27.1% (16/59). Antibody values were higher in the first episode of nephrotic syndrome (HBs antibody: first episode of nephrotic syndrome mean 81.08±31.05 versus follow-up 18.31±13.95, $p<0.002$, t test; IgG for rubella: first episode of nephrotic syndrome median 55.90 (44.40-87.10) versus median follow-up 21.60 (15.35-50.55), $p=0.042$, Mann-Whitney test). There was no correlation between age at disease onset, age at IgG rubella and HBs antibody dosage, interval between age at disease onset and age at antibody dosage or time of last relapse, and HBs antibody values and for IgG rubella, $p>005$, Spearman correlation test. Gender, corticosteroid use or immunosuppressant use were not associated with levels HBs antibody or IgG for rubella, $p>0.05$, Wilcoxon test. Nephrotic patients with frequent relapses had lower levels of antiHBs ($p<0.02$) and IgG for rubella ($p=0.05$), Wilcoxon test.
Conclusion: Previously vaccinated nephrotic patients have low levels of HBs antibody and IgG for rubella, especially in those who have frequent relapses.
The data can improve the follow-up of the nephrotic patient; performing periodic dosages of HBs antibody and IgG for rubella, especially in patients with frequent recurrences so that they can receive the vaccine and, if seropositive, ensure protection against diseases.

Nephrotic syndrome

P3-578 - Retrospective analysis of findings of renal biopsy reports of steroid resistant nephrotic syndrome.

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ABSTRACT
Background -Majority of the patients of nephrotic syndrome, achieve remission after treatment with prednisolone.
According to the latest and current ISPN, IPNA -2020, kidney biopsy is indicated in all SRNS except those with monogenic SRNS.
In this study, we discuss about the clinic-pathological variation reflected in the biopsy reports, response of immunosuppressive drugs and effect of these drugs on the socioeconomic status of patients.
Aim: Analysis of renal biopsy reports of steroid resistant nephrotic syndrome .
Objective: 1) To assess the renal biopsy findings.
2)To study about the response of various immunosuppressive drugs in terms of their cost effectiveness in a tertiary care Centre of a Developing country.
Settings and Design: A 3 year retrospective analysis conducted during the period of January 2019 to January 2022 among paediatric patients attending outpatient department and admitted in Paediatric nephrology department of Dr Prabhakar Kore Hospital and MRC, Belagavi, Karnataka, India.
Result: According to the study, we found that 3 patient showed segmental entrapment on Direct immunofluorescence .
On light microscopy 3 patients showed global sclerosis, 2 showed segmental tuft sclerosis, 3 showed focal dilatation and 1 biopsy report was unremarkable
On electron microscopy 4 patients showed focal effacement,4 patients showed diffuse effacement and 1 patient showed minimal effacement.
Conclusion: For the understanding of FSGS lesions, we need to emphasize on identifying the primary vs secondary/maladaptive nature of focal/segmental sclerosis. Genetic forms of FSGS have variable ultrastructural appearances and need further studies on genetic analysis in suspected cases .
We also found that calcineurin inhibitors (cyclosporine and tacrolimus) constitute the current mainstay of treatment and are not cost effective in resource limited setting as these require long term administration.
Key words: Steroid resistant nephrotic syndrome, renal biopsy, immunosuppressive drugs.

Nephrotic syndrome

P3-579 - The genetic basis of nephrotic syndrome and asymptomatic proteinuria in Japanese population

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Background: Recently, many disease-causing gene variants have been detected in patients with proteinuria, such as steroid-resistant nephrotic syndrome (SRNS), and patients with focal segmental glomerulosclerosis (FSGS) on biopsy. Generally, the rate of variant identification in these patients is only about 30%, but the information about the presence or absence of variants is important for the future therapeutic strategy and predicting prognosis.
Methods: Since 2016, we performed targeted panel sequencing for 556 cases with congenital nephrotic syndrome, infantile nephrotic syndrome, SRNS and asymptomatic proteinuria in Japan. A retrospective review was conducted for these cases.
Results: We detected disease-causing variants for 176 cases (32%). A total of 34 causative genes were identified and the most common identified genes were as follows; *WT1* (20%), *NPHS1* (13%), *TRPC6* (9%), *INF2* (7%) and *LAMB2* (5%).
The variant identification rates were high in congenital (81%) and infantile cases (48%). The rates were lower at 1 year old (14%) and at 2 years old (21%). The rates in other age groups were approximately 30%.
Variants were detected in 39% of asymptomatic proteinuria cases compared with only 19% of SRNS. When restricted to SRNS with rapidly progressive edema, variants were detected in only 8%. In these cases, even with FSGS, variants were detected in only 9%.
Conclusion: We reported a variety of candidate variants identified in patients with nephrotic syndrome and proteinuria in Japan. Even with FSGS on biopsy, the variant identification rate was low in SRNS who showed rapidly developing edema.

Nephrotic syndrome

P3-580 - Analysis of 4 genes mutation (NPHS1, NPHS2, WT1, AND LAMB2) in children with Steroid Resistant Nephrotic Syndrome

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Abstract
Background: A large number of Steroid Resistant Nephrotic Syndrome (SRNS) patients have been reported worldwide due to mutation of NPHS1, NPHS2,WT1 and LAMB2 genes. These cases are usually resistant to steroid as well as other immunosuppressive agents. Hence current study was aimed to determine the mutation of NPHS1, NPHS2, WT1, LAMB2 genes and observed the type of genetic mutation and renal histological pattern of SRNS patients.
Method of study: This cross sectional study was conducted on 25 SRNS patients aged 1year-18 years in the Department of Pediatric Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from July 2017 to June 2018. DNA was extracted from all patients' venous blood lymphocytes using Invitrogen (USA) DNA isolation kit and Next Generation Sequencing(NGS) was done using nephrotic syndrome gene panel (IDT primer, Illinois, USA), aligned to human reference genome (GRCh37/hg19) using BWA program. Mutation analysis was performed after sequencing all exons of NPHS1, NPHS2, WT1 and LAMB2 genes. Histopathological study of renal tissue was performed among 17 patients who gave consent.
Results: Among the study subjects, majority were male(male 56%), mean age 106.32months and mean age of onset of 1st attack of nephrotic syndrome 94.20months. Histopathologically majority (41%) had minimal change disease (MCD). One(4%) study subject had nonsense type of NPHS2 gene mutation on exon 5 who had histopathologically diffuse mesangial proliferative glomerulonephritis and clinically had stage-4 CKD. Another subject (4%) had missense type of COL4A5 gene mutation on exon 37 which was an observational finding and histopathologically had focal segmental glomerulosclerosis. Both of them were male, no family history of renal disease or consanguinity, hematuria and hearing impairment were present.
Conclusion: It was concluded in this study that genetic mutation of SRNS patients above 1 year of age was not uncommon and who had genetic mutation having bad histopathological variety.

Nephrotic syndrome

P3-583 - Serum miRNAs in childhood idiopathic nephrotic syndrome

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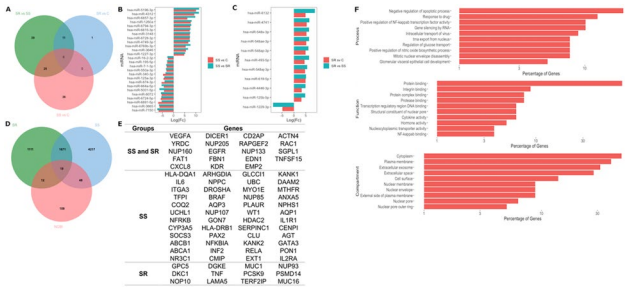
Introduction: miRNAs are non-coding RNA that are recently recognized as biomarkers of kidney disorders. We examined differentially expressed miRNA and their targets in patients with steroid-sensitive and steroid-resistant nephrotic syndrome (NS).
Methods: We enrolled patients, 2-18-year-old, with steroid-sensitive NS, either at onset or relapse, and steroid-resistant NS, at diagnosis of steroid-resistance. Patients with steroid-sensitive NS were off any immunosuppression while those with steroid-resistance were on therapy with prednisolone at enrolment. Controls were otherwise healthy children attending outpatient for vaccination or for minor non-infectious non-renal ailments. Following RNA extraction using RNeasy (Agilent, Santa Clara, CA), differential expression of 2549 miRNAs was examined using the Agilent G3 miRNA 8x60k microarray kits. Using the LIMMA package in R (Vienna Austria), differentially expressed miRNA were identified as miRNA with absolute $\log_2$ fold change by >2 and adjusted P <0.05. Target genes, predicted using miRNet (https://www.mirnet.ca/), were compared against the genes for NS in the NCBI database, and the ontology of selected genes was examined using DAVID (https://david.ncifcrf.gov/summary.jsp).
Results: Comparison of miRNA expression in 20 patients and 11 controls led to the identification of 62 and 12 differentially expressed miRNA in patients with steroid-sensitive and steroid-resistant NS, respectively. Of 75 miRNAs differentially regulated in patients with

NS, (Fig 1A), 26 were unique to steroid-sensitive SNS and 11 to steroid-resistant NS (Fig 1B; C). Of 5955 and 2813 genes targeted by the miRNAs specific to steroid-sensitive and steroid-resistant NS, respectively, 79 were relevant to NS from among the 187 genes reported in context of NS in the NCBI database (Fig 1D, E). Fig. 1F indicates the ontology of these genes.

Conclusion: Steroid-sensitive and steroid-resistant NS have distinct miRNA expression profiles that can be examined for their role as biomarkers and in pathogenetic pathways.



Nephrotic syndrome

P3-584 - Treatment of edema in childhood nephrotic syndrome

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Background: Edema in childhood nephrotic syndrome can be distressing and lead to complications such as skin breakdown and cellulitis.. There is significant variation in management due to concerns over the safety of albumin infusion.
Objective: To assess the safety and efficacy of albumin infusion followed by diuretics therapy (alb+diuretics) for edema in childhood NS.
Design/Methods: Hospitalizations of patients with primary NS diagnosed between 1-17y at pediatric hospitals in Atlanta, Georgia, USA between 2018-2020 were reviewed. Patients with ESKD and kidney transplant were excluded. We described prescription pattern, (alb+diuretics dose, albumin infusion rate, treatment frequency and length of stay (LOS). Efficacy was assessed by percent change in weight pre and post therapy. Treatment complication frequency was reported as percentages of hospitalizations with adverse events due to alb+diuretics therapy. We assessed adverse events including seizures and altered mental status, acute rise in BP >95th% necessitating anti-hypertensive therapy or pause in alb+diuretics, pulmonary edema, respiratory distress, intubation, hypokalemia requiring potassium replacement, and ICU care.
Results: 146 patients (256 hospitalizations) received alb+diuretics for edema. Mean albumin dose was 0.4g/kg (SD= 0.1) infused over 60 minutes in 65% of hospitalizations followed by IV furosemide, 0.8mg/kg (SD=0.3). The therapy was given every 8h in 84% of hospitalizations. Mean treatment duration was 2.2 days (SD=1.6). Mean hospital LOS was 3.1 days (SD= 2.0). Mean change in weight was 7.4% (SD= 6.0). The most common complication was acute rise in BP (20% of hospitalizations, Table 1). Only 1 hospitalization required ICU care for elevated BP and pulmonary edema. The patient was placed on a nicardipine drip and 1L low-flow nasal cannula.

Table 1: Frequency of albumin and diuretics therapy complications for edema treatment in children with primary nephrotic syndrome.

Complication	% Hospitalizations *[n hospitalizations]*
Seizures or altered mental status	0
Acute Rise in Blood Pressure	20% (n=51)
Pulmonary Edema	0.4% (n=1)
Hypokalemia	12% (n=31)
ICU care	0.4% (n=1)
Intubation	0

Conclusion: Alb+diuretics therapy was effective for diuresis in children with edema due to primary NS and complication frequency was relatively low. This suggests that alb+diuretics therapy can be safely used to treat edema in childhood NS.

Nephrotic syndrome

P3-585 - Infantile SRNS associated with LAMA5 mutations

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Steroid-resistant Nephrotic Syndrome (SRNS) is a subtype of nephrotic syndrome characterized by proteinuria, hypoalbuminemia, and edema that does not respond to steroid therapy. Single gene pathogenic mutations have been implicated in up to 30% of pediatric SRNS, and over 70 genes have been reported to date. Of those recently discovered is *LAMA5*, which encodes the laminin-alpha-5 chain. Forming the laminin $\alpha5\beta2\gamma1$ hetero-trimer, it is not only an essential component of the glomerular basement membrane (GBM) but also important for embryogenesis and immune modulation. Homozygous or compound heterozygous variants of *LAMA5* have been identified to date in ten pediatric NS patients with variable phenotypes. These patients had onset of NS ranging from 3 months to 8 years. Response to therapy and renal outcomes varied from steroid sensitive NS to early end-stage kidney disease (ESKD).Biallelic truncating mutations of this gene were proven to cause SRNS recently.
Here we present a case of infantile SRNS related to compound heterozygous variations of *LAMA5* (c.3434G>A, p.Cys1145Tyr and c.6883C>T, p.Gln2295*). A 10-month-old female presented with eyelid edema and massive proteinuria without any extra-renal symptoms or family history. She was diagnosed with SRNS and renal biopsy revealed focal segmental glomerulosclerosis with widely effaced epithelial foot processes and "moth-eaten" appearance of GBM. She progressed to ESKD requiring dialysis at 3 years and 5 months of age, and received deceased-donor kidney transplant at 6 years of age. 4 months after transplantation, she developed EBV-related post-transplant lymphoproliferative disease (PTLD), which was treated with chemotherapy. While our case has one missense and one truncating allele, her phenotype is similar to those with biallelic truncating variants, possibly because her missense variant alters splicing. Whether *LAMA5* defects has played a role in vulnerability to PTLD is yet to be investigated.
This case provides additive evidence that *LAMA5* variants are related to SRNS.

Nephrotic syndrome

P3-586 - Role of serum osteocalcin in patients of nephrotic syndrome: a comparison of ssns and srns children

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Background: Long term use of corticosteroids tends to reduce osteoblastic activity and formation of matrix constituents; Osteocalcin (OS), a bone turnover marker has a greater sensitivity than alkaline phosphatase for bone matrix synthesis.
Aims and Objectives: The primary objective of study was to evaluate the bone mineral metabolism by measuring vitamin D, PTH and osteocalcin levels in children and adolescents (2-18 years) with nephrotic syndrome during remission. The secondary objectives were comparison of biochemical parameters between SSNS and SRNS children and their correlation with disease type, doses and duration of steroid therapy and anthropometry.
Materials and Methods: This cross-sectional study was done between Jan 2021- Sep 2021; total of 62 (40M, 22F) children (32 SSNS and 30 SRNS) were enrolled. Children with CKD, those having received daily steroids or mega doses of Vitamin D in last 3 months were excluded.
Results: The clinical and biochemical parameters are shown in the Table**.** Amongst SSNS patients, 46.8% had vitamin D insufficiency, 21.9% had deficiency. In the SRNS group, 40% patients had insufficiency and 33.4% had deficiency. Serum osteocalcin levels were found to be significantly lower in SRNS patients 20.4 (10.8, 33.5) compared to SSNS patients, 35.6 (22.5, 42.7), p=0.004. There was a negative correlation between steroid dose and serum osteocalcin levels, p=0.152.
Conclusions: The SSNS and SRNS patients had vitamin D deficiency and insufficiency, where an expected response would be a rise in the serum osteocalcin levels. However, the levels were found to be lower for age, with the values being significantly lower in the SRNS patients. This reflects the suppressive effect of steroids on the bone lay down activity. Serum osteocalcin can thus serve as a useful noninvasive tool for assessing bone metabolism and the impact of long-term steroids on overall bone health.

Table: Comparison of biochemical parameters of SSNS and SRNS patients

Parameter	SSNS (n = 32) Median (IQR)	SRNS (n = 30) Median (IQR)	P values
Age at enrollment (yrs)	7.5 (5.2, 11)	10 (7, 12)	<0.006*
Disease duration (yrs)	3 (2, 5)	6 (2.5, 9.0)	0.167
Type of disease (%)	SDNS 9 (28.1%) FRNS 13(40.6%) IFRNS 10 (31.3%)	Initial resistance 8 (26.7%) Late resistance 22 (73.3%)	
Steroid dose in last 6 months (mg/kg/day)	0.50 (0.32, 0.60)	0.63 (0.35, 0.77)	0.02*
Serum Albumin (gm/dL)	3.15(2.8, 4.0)	3.1(2.8, 3.5)	0.054
Serum Cholesterol (mg/dL)	144(124, 176)	194(147.2, 301.5)	0.026*
Serum Calcium	9.2(8.8, 9.6)	9.1(8.6, 9.3)	0.69
Serum Phosphate	4.6(4.1, 5.4)	4.7(3.9, 5)	0.173
Serum ALP	156.5(115.2, 190.5)	139(111.7, 186.5)	0.004*
Serum Osteocalcin (µg/L)	35.6(22.5, 42.7)	20.4(10.8, 33.5)	0.004*
PTH levels	38.4(27.5, 58.4)	56.1(45.6, 83.7)	0.009*
25(OH)D levels (ng/ml)	24.9(20.2, 29)	26.6(18.47, 29.73)	0.968

Nephrotic syndrome

P3-587 - Non-coding RNA 886 plays a role in the development of minimal change nephrotic syndrome.

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Introduction: Minimal change nephrotic syndrome (MCNS), a major cause of nephrotic syndrome in children, is characterized by massive proteinuria. Humoral factors produced by immune cells, such as T lymphocytes, have been indicated to disrupt the filtration barrier thereby increasing protein permeability in glomeruli. Previously, using the Infinium Human Methylation 450 array, we detected that DNA methylation ratio in the non-coding RNA 886 (nc886) gene region of helper T cells (THs) was significantly different between MCNS patients and controls, and that nc886 expression in THs was significantly low at relapse compared with that at remission and in healthy controls. To elucidate MCNS pathogenesis, in this study, we tested whether nc886 induces podocyte dysfunction, eventually causing proteinuria.
Methods: We investigated DNA methylation status of the nc886 gene in conditional immortalized human podocytes (cipods) using bisulfite-pyrosequencing. Cipods were stimulated with poly I:C and lipopolysaccharide as infection models, and with patients' serum derived at relapse and remission as the MCNS model. Expression of nc886 was measured using rt-PCR.
Results: The methylation level at the nc886 gene in cipods was rather high. There were no significant differences in methylation status at the region before and after cipods differentiation. In the infection models, nc886 expression in cipods tended to decrease at 1 h after stimulation and recover after 3–6 h. In the MCNS model, nc886 expression was significantly higher in cipods stimulated with remission than with relapse serums.
Discussion: Decrease in nc886 expression indicates a general pathologic state of cells. In cipods, nc886 expression showed the same trend as that in THs from patients between relapse and remission. This indicates that the same factors in patients' serum at relapse may induce change in nc886 expression in both THs and cipods regardless of nc886 gene DNA methylation status.

Nephrotic syndrome

P3-588 - Short-term prednisolone treatment for first episode of childhood nephrotic syndrome with rapid remission: a prospective, cohort study

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Background and objective: Idiopathic nephrotic syndrome (INS) is the most common glomerular disease in childhood and corticosteroid therapy is its most effective treatment. Appropriate duration of initial corticosteroid therapy is an important issue in INS due to concerns over side effects of its prolonged administration versus the risk of relapses with inadequate treatment. Our study is to test the feasibility of a shorter duration of corticosteroid therapy in newly diagnosed patients with INS who show a quicker treatment response.

Study design: A prospective, open-label, observational clinical cohort study was conducted. Patients who respond within 10 days (Group A) will receive a total of 8 weeks of corticosteroid therapy versus ≥12 weeks in those who respond between 10 days to 28 days (Group B), and were followed up for 52 weeks after initial therapy duration. The primary endpoint is time to first relapse in days.
Results: A total of 33 INS children were enrolled in this study, and the follow-up data of 30 patients were analyzed with 2 patients drop out. The clinical and laboratory characteristics of patients in both groups were similar. No significant difference was found in time to first relapse [65(14.5, 159) days for group A vs 28(17, 61.5) days for group B, Log Rank *P=0.0.371*], the incidence of frequently relapsing nephrotic syndrome [group A 6/18 (33.3%) vs group B 5/10(50%), *P=0.644*] . Group B received similar corticosteroid dose compare with Group A during study priod (2586±1810 mg/m^2 versus 2559±1461 mg/m^2, *P=0.968*). Frequency and severity of corticosteroid-related complications was similar in both groups and it's not obvious overall.
Conclusion: A shorter 8 weeks' initial corticosteroid regimen can be used in SSNS children with rapid remission(≤10 days). Our outcomes provide first evidence of determine the appropriate duration of corticosteroid therapy for first episode in childhood INS base on patient's characteristics.

Nephrotic syndrome

P3-589 - High incidence of pediatric idiopathic nephrotic syndrome in Miyako Island, southwest Japan

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Background: The incidence of idiopathic nephrotic syndrome (INS) varies among countries with a higher incidence in Asia than in Europe and the United States. We investigated the incidence and clinical features of INS on Miyako Island, located in southwest Japan, to determine its epidemiological characteristics.
Methods: We performed a retrospective review of new pediatric INS cases between 2005 and 2021 in individuals aged 6 months to 15 years residing on Miyako Island. Children with congenital nephrotic syndrome and nephrotic syndrome secondary to nephritis were excluded. We used a population-based denominator from demographic data to estimate the annual INS incidence. Clinical data were collected from medical records.
Results: Thirteen children (9 male) were newly diagnosed with INS on Miyako Island between 2005 and 2021. All patients were of Asian ethnicity. The mean annual incidence was 9.3/100,000. Steroid-sensitive nephrotic syndrome was found in 11 (85%) and steroid-resistant nephrotic syndrome in 2 (15%) patients. At the last follow-up, one patient (8%) was older than 18 years and still had active disease.
Discussion/Conclusion: The incidence of INS in Miyako Island was higher than in other countries and Japan as a whole (6.49/100,000). Genetic background may be a reason for this high incidence, as the island has a relatively isolated population. However, as in epidemiological disease studies, the incidence of INS in Japan may show the pattern expected for a dual structure model. In addition, Miyako Island is an area with a high frequency of nephrotic syndrome. A variant with a strong influence may be genetically conserved.

Nephrotic syndrome

P3-590 - The role of calcineurin inhibitors in monogenic steroid resistant nephrotic syndrome: a multicentre retrospective study

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Calcineurin inhibitors (CNI) are recommended as first line immunosuppression in pediatric steroid resistant nephrotic syndrome (SRNS), but their use is not advocated for mendelian disease. However, accumulating evidence suggests that these agents can induce remission and improve kidney outcome in selected cases. We aimed to retrospectively study the frequency of remission, its possible predictors and impact on kidney outcome in children with monogenic SRNS treated with a CNI. Children with proven monogenic SRNS aged 0-18 years treated with a CNI for at least 3 months were eligible for inclusion. Demographic, clinical, biochemical, histopathological, genetic and treatment information at distinct time points were collected: (i) at diagnosis; (ii) at CNI treatment onset; (iii) at 6, 12 and 24 months of CNI treatment; and (iv) at last visit available or at initiation of kidney replacement therapy (KRT). A dedicated geneticist reviewed all reported variants according to current American College of Medical Genetics guidelines and only children with *pathogenic* and *likely pathogenic* genotypes were included in the analysis. Data of 141 subjects (pathogenic genotype N=122 and likely pathogenic genotype N=19) from 37 pediatric nephrology centres were analyzed. After 6 months of treatment and at last visit, a partial or complete remission was documented in 27.6% and 22.5% of cases respectively. Achieving at least partial remission at 6 months of treatment and at last visit conferred a 75% and 97% less risk of kidney failure (hazard ratio [95%CI] 0.25 [0.1- 0.6]; P=0.003

and 0.03, [0.002- 0.52]; P=0.02, respectively). Among various clinical, biochemical, histopathological and genetic parameters only higher serum albumin level at CNI initiation could predict remission at last visit (odds ratio [95% CI] 2.8, [1.1- 6.9]; P=0.02). Our findings are supportive of a trial course of CNI in children with monogenic SRNS with close surveillance of proteinuria evolution and possible side effects.

Nephrotic syndrome

P3-592 - Glucocorticoid administration and changes in bone turnover markers in pediatric idiopathic nephrotic syndrome

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Background: There are few reports on changes in bone turnover markers (BTMs) under glucocorticoid (GC) administration and after discontinuation of GC in pediatric nephrotic syndrome.
Methods: Among patients with childhood-onset idiopathic nephrotic syndrome who received the first administration of rituximab between January 2015 and March 2021, those whose BTMs were measured under GC administration and after discontinuation were included. The relationship between GC administration and changes of BTMs was retrospectively evaluated. Bone alkaline phosphatase (BAP) and intact procollagen type 1 N-terminal propeptide (P1NP) were used as bone formation markers, and tartrate-resistant acid phosphatase 5b (TRACP-5b) was used as a bone resorption marker.
Results: Twenty-eight patients were included, and 37 BTM pairs with and without administration of GC were analyzed. The mean age at BTM measurement under GC administration was 11.9 ± 3.3 years, and the mean time from the onset of nephrotic syndrome to the measurement of BTMs under GC administration was 7.3 ± 3.3 years. The mean duration from GC discontinuation to the measurement of BTMs was 3.5 ± 1.0 months. Regarding BAP SD score, intact P1NP SD score, and TRACP-5b, there were no significant changes in any of the BTMs after GC discontinuation when the daily prednisolone (PSL) dose at BTM measurement was < 0.25 mg/kg/day (BAP SD score, $p = 0.34$; intact P1NP SD score, $p = 0.70$; TRACP-5b, $p = 0.78$). When the daily PSL dose at the measurement of BTMs was ≥ 0.25 mg/kg/day, all BTMs were significantly increased after GC discontinuation (BAP SD score, $p < 0.0001$; intact P1NP SD score, $p < 0.0001$; TRACP-5b, $p < 0.0001$).
Conclusions: These data suggest that suppression of bone metabolism can be released by discontinuing GC even after several years of administration. Additionally, low daily doses of GC may have less effect on bone metabolism.

Nephrotic syndrome

P3-593 - Low post vaccine antibody titers in idiopathic nephrotic syndrome children treated with rituximab

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Introduction: Infections remain a major complication in children with idiopathic nephrotic syndrome (INS). We report post-vaccination antibody levels for hepatitis B, measles, diphtheria, tetanus, and varicella in patients with steroid dependent INS treated with rituximab (RTX).
Patients and Methods: We carried out a retrospective study in the pediatric nephrology units of Trousseau, Necker and Robert Debré hospitals. All children with INS and treated with RTX were included. Post vaccine Ab titers and the following clinical and biological parameters were analyzed: age at INS diagnosis, number of relapses before and after RTX, duration of INS, other immunosuppressive treatment, immunoglobulin levels, duration of B cell depletion, time between the last RTX dose and time interval between the last relapse and post-vaccination serologies. The primary endpoint was a positive antibody titer.
Results: 37 patients were included. The median age at INS diagnosis was 3.5 (2.5-6.3) years, the median duration of the INS was 9 (5.0-12.5) years, the median time between the last relapse and post-vaccination serology sampling was 17 (6.5-31) months, the median IgG level was 8.3 (6.6-10.4) g/L. 23/37 (62%) patients received calcineurin inhibitors during disease course, 25/37 (67%) received MMF, 15/37 (40%) received both and 24/37 (65%) received Levamisole. The median duration of B cell depletion was 7.5 (3.3-11.5) years and the time between the last RTX dose and vaccine serologies was 14 (6-29) months. The percentage of positive vaccine titers for hepatitis B, measles, diphtheria / tetanus and chickenpox were 35%, 62%, 48% and 32%, respectively, all lower than in healthy children. When compared to INS patients on oral drugs without RTX, the percentages of positive titers were the same for hepatitis B and measles, but lower for diphteria/tetanus and varicella (85%-83%).
Conclusion: INS patients treated with RTX had low post-vaccination antibody titers, which were not related to any other specific treatment modality.

Nephrotic syndrome

P3-594 - Levamisole modulates podocytes' actin cytoskeleton in vitro in nephrotic syndrome

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Podocytes are key target cells of glomerular diseases such as nephrotic syndrome (INS), where nephrotic proteinuria and podocyte injury plays a central role in its pathophysiology. Glucocorticoids are the gold standard therapy intervention for INS. Nevertheless, frequent relapses are common in children. Glucocorticoids are often combined with steroid-sparing agents to avoid prolonged steroid-use and reduce

steroid toxicity. Levamisole is one of these steroid-sparing drugs, which has shown to reduce the number of relapses and maintain remission in children with INS. Although clinical effectiveness of levamisole has been demonstrated, the molecular mechanisms how levamisole exerts its beneficial effects remains poorly studied. Therefore, we aim to elaborate on the effects of levamisole on human podocytes in NS. RNA sequencing data from human podocyte cell line treated with levamisole 1 µM for 24 hours indicate that levamisole exert its therapeutic effects in podocytes by regulating genes related to the actin cytoskeleton processes and signaling. Levamisole-treated podocytes showed significant up- or downregulation of *SHROOM2, PLAUR, ARHGAP6,SEMA7A, ITG4, and ITG8* genes, all related to actin cytoskeleton remodeling. Functional experiments show that podocytes exposed to puromycin aminonucleoside (PAN; 60 µg/mL), lipopolysaccharides (LPS; (1-10-20-40 µg/mL)), NS patient plasma at active state (n=3) resulted in significant actin cytoskeleton derangement and reduced cell motility when compared to controls. Moreover, levamisole prevented PAN-, LPS-, and NS patient plasma-induced actin cytoskeleton damage on podocytes *in vitro* and increased cell motility. In conclusion, our data show that levamisole exerts its beneficial effects on podocytes by stabilizing the actin cytoskeleton through promoting pivotal actin cytoskeleton signaling and processes highly important for the maintenance of functional glomerular filtration barrier.

Nephrotic syndrome

P3-595 - Plasma exchange or immunoadsorption for recurrent focal segmental glomerulosclerosis: clear differences in vitro

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Primary focal segmental glomerulosclerosis (FSGS) is one of the most common glomerular diseases in children, characterized by therapy resistant nephrotic proteinuria leading to deterioration of kidney function. Plasma circulating permeability factors (CPFs), of which the nature and origin are still unclear, have been postulated to play an important role in FSGS' disease pathology due to frequent posttransplant recurrence of proteinuria, and response to immunoadsorption (IA) and plasma exchange therapy (TPE). *In vitro*, CPFs from plasma of FSGS patients causes excessive reactive oxygen species (ROS) formation in podocytes, which eventually results in podocyte cell death. The effectiveness of IA may suggest that the CPF could be a circulating immunoglobulin (Ig) or lie in the Ig fraction. Here, we aimed to purify Ig fractions from the plasma of FSGS patients with presumed CPFs and investigate their effect on podocytes *in vitro*. SDS-PAGE confirmed two bands of 25 and 50 kDa for the purified Ig fractions isolated from three FSGS patients with presumed CPF, one FSGS patient at remission, two non-renal control patients, and healthy controls using a protein A/G affinity chromatography column. Interestingly, our results show increased ROS levels and cell death in podocyte in response to flow-through fractions and not in response to Ig fractions. Elevated ROS levels and podocyte cell death was observed solely in response to flow-through fractions obtained from the three FSGS patients with presumed CPF. In conclusion, we show that a putative CPF associated with FSGS does not seem to lie in Ig fractions of the three patients studied, which may suggest that solely IA is not enough to efficiently remove CPFs from plasma.

Nephrotic syndrome

P3-596 - Evaluating the long-term outcome of Childhood Nephrotic Syndrome

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Background: Idiopathic childhood nephrotic syndrome is a rare disease with a prevalence of 15-17 per 100,000 children. Information on long-term outcomes are required when informing carers of treatment options during disease course in childhood. Furthermore, a history of clinically evident kidney disease in childhood is associated with increased risk of end stage renal failure in adulthood. Few studies exist describing long-term outcome of nephrotic syndrome.
Methodology: An observational cohort study involving patients discharged from the paediatric nephrotic clinic at Great Ormond Street Hospital to the Nephrology service at the Royal Free Hospital between 1980-2021 was undertaken. Children presenting with idiopathic steroid sensitive nephrotic syndrome were included in this study. Patients with syndromic and monogenic steroid resistant nephrotic syndrome were excluded in addition to secondary causes with renal involvement.
Results: Of over 600 patients identified from GOSH nephrotic clinic since 1980, we undertook a pilot study to assess feasibility of data extraction in 49 patients referred to a local adult nephrotic clinic.16 patients were lost to follow up following referral and therefore, have been excluded. Of the 33 patients who had follow up data available (median duration of follow up of 17 (IQR: 10.8, 21.9) years), 12 were males and 21 females. In total, 17 patients (51.5%) continued to relapse in adulthood and 3 patients developed CKD. In childhood, glomerulosclerosis was found in 11 patients, who had a median eGFR of >90(15,90) mls/min/1.73m^2 at last follow up, MCD in 11 and IgM nephropathy in 1 patient. Only 7 patients had a repeat biopsy in adulthood. In childhood, the median number of drugs used per patient to induce or prolong remission was 3(2,4), while in adult care it was 2(1,3).
Conclusion: Our cohort study is ongoing and will support collaborative studies to inform assessment of long-term outcome of childhood nephrotic syndrome.

Nephrotic syndrome

P3-597 - A rare case of collapsing variant of focal segmental glomerulosclerosis in an eight-year old female Filipino child

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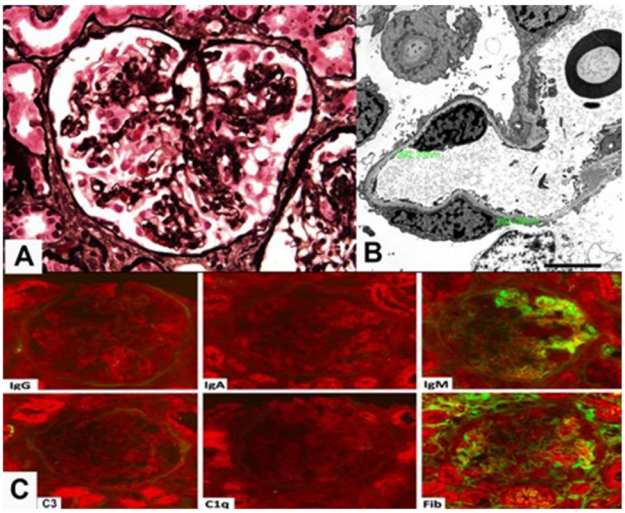
Collapsing Glomerulopathy is a distinct aggressive subset of focal segmental glomerulosclerosis. Usually seen in patients with human immunodeficiency virus (HIV) infection, presentation in children without any evidence of such is of considerable interest. We report a case of an eight-year old female Filipino child who presented with

a three-month history of intermittent edema, hypoalbuminemia, and proteinuria. Based on the presentation, a diagnosis of nephrotic syndrome was made. Other laboratory results revealed hypercholesterolemia, hypocalcemia, and severe Vitamin D deficiency. To rule out the probability that the patient actually has unrecognized HIV-associated nephropathy, seronegativity for HIV infection was documented. The patient was initiated on a four-week course of full-dose oral prednisone and Enalapril but did not achieve remission. High-dose intravenous methylprednisolone pulsing was also given but patient still had no response. Following ultrasound-guided renal biopsy, histopathological findings of collapsing glomerulopathy were seen.



Combined treatment with steroids, oral cyclosporine resulted in significant improvement of edema and decreased proteinuria. This variant is described to have an increased risk of progression to end-stage renal disease. Conversely, children that achieve partial or complete remission have been documented. Patients with this subset of difficult-to-treat nephrotic syndrome should be screened for underlying etiology and introduced with a trial of immunosuppressive treatment.

Nephrotic syndrome

P3-598 - Incidence of hypertension in children with nephrotic syndrome

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Introduction: Incidence of hypertension among children with steroid sensitive (SSNS) and frequently relapsing nephrotic syndrome (FRNS) is still unknown. We determined the incidence of hypertension in children with nephrotic syndrome defined by treatment response and associated risk factors.
Method: The Insight into Nephrotic Syndrome study is a prospective observational cohort study of children with idiopathic nephrotic syndrome, ages 6 months to 18 years old, followed at The Hospital for Sick Children and local community hospitals in the greater Toronto Area. Clinical data were abstracted from electronic medical records with double data entry. Steroid resistance or steroid response was determined after initial prednisone therapy and frequently relapsing course had >2 relapses at 6 months. Risk factors included sex, family history, and body mass index (BMI). Hypertension was diagnosed as blood pressure >= 95th percentile (for age, sex and height) on three consecutive clinic visits or if patients received antihypertensive medications.
Results: A total of 552 children diagnosed from 1996 until 2018 were included with a median follow-up of 4.2 years. Mean age at presentation was 3.7 years, 63% were male and reported ethnicities were 41% Asian, 26% European and 33% others. 521 presented with SSNS (113 had FRNS). Cyclophosphamide was prescribed most often for FRNS/SSNS and tacrolimus for SRNS. Overall, 5.6% participants developed hypertension at a median of 24.8 months with an incidence rate of 0.30 per 10,000 person-years [95% confidence interval (CI): 0.21, 0.43]. Proportion of hypertension among those children with FRNS was higher at 9.7% and 16.1% with SRNS. No risk factors were associated with development of hypertension (sex, BMI, ethnicity, or familial history).

Table: Incidence of hypertension by treatment response and relapsing status

Initial steroid response	**SSNS (n=521)**	**SRNS (n=31)**
Hypertension, n (%)	26 (5.0)	5 (16.1)
Incidence rate[a], [95% CI]	0.27 [0.18, 0.39]	0.90 [0.38, 2.17]
Relapsing status	**Infrequently relapsing (n=408)**	**Frequently relapsing (n=113)**
Hypertension, n (%)	15 (3.7)	11 (9.7)
Incidence rate[a], [95% CI]	0.21 [0.12, 0.35]	0.44 [0.24, 0.79]

[a] Per 10,000 person-years

Conclusion: Overall incidence of hypertension among children with NS is quite low, although there is a higher incidence in a graded manner among those with FRNS at 6 months and initial steroid resistance.

Nephrotic syndrome

P3-599 - Value of pathological features and PLA2R in children with primary membranous nephropathy

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Objective: To explore the value of pathological features of atypical membranous nephropathy and PLA2R in diagnosis and treatment of children with primary membranous nephropathy (PMN).
Methods: A retrospective study was conducted in children (<18 years) with biopsy-proven PMN without secondary causes.
Results: Study cohort included 33 (M:F ratio 1.54:1) patients and median age 11 (ranged 3-16) years. There was nephrotic-range proteinuria in 32 cases, hematuria in 24 cases, hypertension in 8 cases at the onset, and thrombosis in 2 cases. Renal biopsy was performed 0.6~78.1 months after onset, and 28 patients (84.8%) received glucocorticoid and/or immunosuppressive therapy before renal biopsy. The pathological manifestations presented with typical MN in 18 cases and atypical MN in 15 cases. There was no statistical difference in clinical manifestations and prognosis between the two groups. 20 cases (60.6%) were PLA2R related. Compared with non-PLA2R-related

group, PLA2R-related group had older age of onset (median age 12 vs. 7 years, P=0.011), lower prodromic infection rate (45% vs. 84.6%, P=0.032), and lower spontaneous response rate (0 vs. 30.8%, P=0.017). The PLA2R-related group also had a higher proportion of hypertension at onset, urine protein quantification at renal biopsy, venous thrombosis, and pathological manifestations of typical MN, but there was no significant statistical difference. PLA2R positivity in renal tissue was significantly associated with primary/co-deposition of renal IgG4 and low albumin levels at renal biopsy. Recurrent urinary protein was found in children with positive serum PLA2R antibody during follow-up.
Conclusions: Tests for PLA2R should be performed to confirm the PLA2R-related MN diagnosis, especially for adolescent patients. Regular tests for serum PLA2R during follow-up in these patients may help to detect disease activity and guide the treatment.

Nephrotic syndrome

P3-600 - Prevalence of Thromboembolic Events in Children with Nephrotic Syndrome: A Systematic Review and Meta-Analysis

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Background: Nephrotic syndrome (NS) is a common kidney disease of childhood, affecting 2-7 children per 100,000. Thromboembolism (TE) is a potentially life-threatening complication among children with NS. There remains a paucity of information regarding the burden of TE and its associated risk factors in this population.
Methods: A systematic literature search screening was conducted on four electronic databases to include relevant full-length publications, published abstracts and conference proceedings written in English language from Jan 1974 to May 2021. Article, data extraction and quality assessment were independently completed and verified by two reviewers. Meta-analysis was conducted on the prevalence of TE in children with all forms of NS and in children with congenital NS.
Results: Of 13,626 screened studies, 23 studies and 13,933 total subjects (ages ranging from neonates to 21 years) were included for analysis. The pooled prevalence of symptomatic TE among patients with NS was 3.64% (95% CI 2.18-5.86), which increased to 8.20% (95% CI 4.09-13.24) in patients with congenital NS. The most common location of TE was in the deep veins of the leg and arm, accounting for 23% and 7% of all TE events; renal vein TE was the third most common location. Children with steroid-resistant NS were at a higher risk of TE compared to steroid-sensitive children (OR 4.40, 95% CI 1.34-15.59, p= 0.013). Focal segmental glomerulosclerosis (FSGS) was the most common histology present in patients with TE (51.2%).
Conclusion: Children with NS are at increased risk for TE, which can be life- or limb- threatening. Risk factors such as congenital NS, steroid resistance and FSGS further elevate risk of TE. Future research is required to identify children with NS who would benefit from prophylactic anticoagulation.

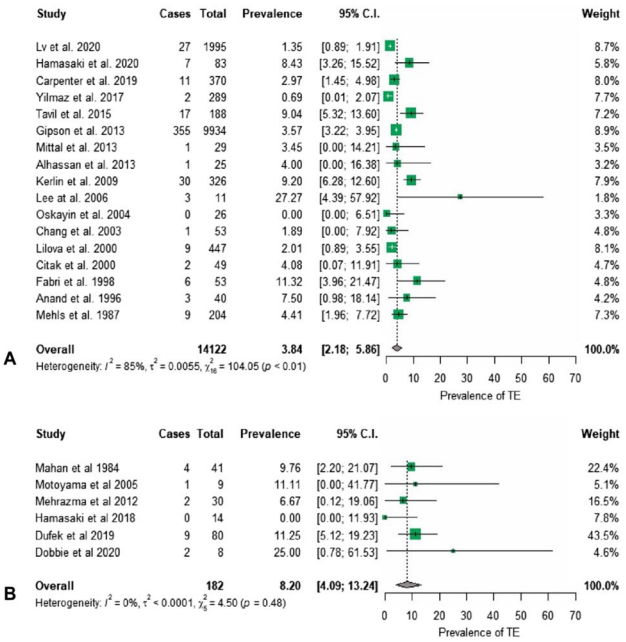

Figure 1: Pooled prevalence of thromboembolism in all forms of nephrotic syndrome excluding congenital nephrotic syndrome (A) and in congenital nephrotic syndrome (B).

Nephrotic syndrome

P3-601 - Adverse events following rituximab infusion in children with nephrotic syndrome: a systematic review and meta-analysis

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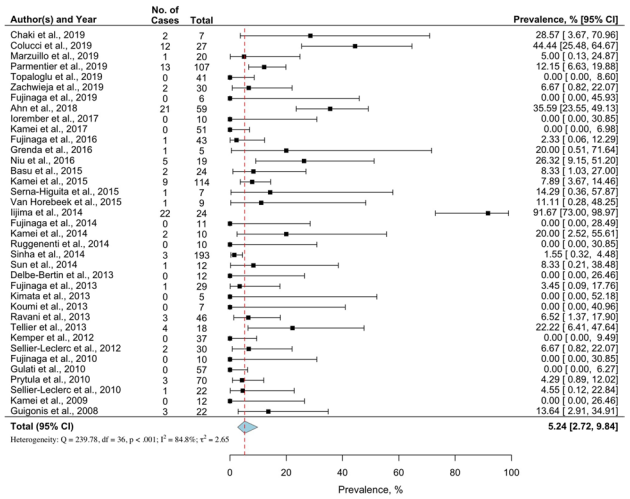
Background: Rituximab is an important treatment option in children with complicated cases of nephrotic syndrome (NS). However, there remains a lack of data on the adverse events and side effects (AE/SE) following rituximab therapy in this population.
Methods: Six databases were searched from 1991-2019 for articles providing AE/SE data on children (≤18yrs) receiving rituximab. Article screening was performed independently by two reviewers, followed by data extraction and quality assessment by three reviewers. The primary outcome was the cumulative prevalence of AE/SE. Secondary outcomes included the severity, timing, and duration of AE/SE. Meta-analyses were performed on the best reported AE/SEs using

a generalized linear model which included all studies that explicitly mentioned the AE/SE. Subgroup analysis of the mean age at the time of rituximab therapy was also performed.

Results: Out of 3364 citations, 57 full-text articles were included (6 RCTs). This review found that the pooled prevalence in all studies reporting infusion-related reactions (n=32) was the highest at 23.33% (95% CI, 15.14-34.16), followed by hypogammaglobulinemia (n=10) (11.23%, 3.35-31.56), infection (n=37) (5.24%, 2.72-9.84) (Figure 1), and neutropenia (n=25) (4.82%, 3.17-7.28). Interestingly, the prevalence of neutropenia was significantly higher (p=0.01) in studies with an older sample age (>10 years, n=9) (7.98%, 5.63-11.18) compared to younger samples (≤10 years, n= 7) (3.27%, 0.99-10.29), while the prevalence of infections was conversely higher in younger children (13.94% vs. 3.64%) but not significantly different (p=0.545). The severity, timing, and duration of AE/SE were heterogeneously reported or frequently incomplete, and often indeterminable.

Conclusion: This review hopes to better inform decision-making for both patients and clinicians. The impact of follow-up duration and cumulative rituximab dosage on AE/SE needs to be further explored, and future studies with standardized reporting of AE/SE timing, duration, and severity grade are strongly warranted.

Figure 1: Pooled prevalence of infections in children with NS following rituximab administration



Nephrotic syndrome

P3-604 - ERICONS – Early RITUXIMAB in Childhood Onset Nephrotic Syndrome – study protocol

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Objectives: Treatment protocols for idiopathic nephrotic syndrome (INS) are based on steroid therapy and a variety of oral steroid sparing immunosuppressive agents for those who follow a protracted steroid dependent (SDNS) or frequently relapsing (FRNS) course. Subjects with SDNS/FRNS are at risk of frequent hospitalizations and numerous side effects of both steroid and immunosuppressive treatment given over many years sometimes throughout childhood. Rituximab, an anti-CD20 antibody has raised hopes of both higher cure rates and decreased treatment related morbidity. Randomized trials on the efficacy of early rituximab treatment of SDNS/FRNS in children are lacking.

Methods: A multicentre, randomized double blinded study was designed for children with SDNS/FRNS to assess the efficacy and safety of early treatment with rituximab prior to any traditional immunosuppressive therapy. Recruitment has started at 9 major University Hospitals. 60 children will be randomised following remission of NS achieved with steroids -30 to rituximab in two weekly infusions of 375mg/m2 and 30 to placebo. The primary endpoint of the study is the time of survival without relapse in the double blinded phase. The secondary endpoints are: time to treatment failure, total dose of steroids and correlation of relapse with lymphocyte B counts, rituximab levels, presence of anti-rituximab antibodies and the subjects' immunofenotype and genotype. Urine and blood tests will be collected during screening and at monthly control visits for a 12 months observation period. Adverse effects of treatment will be monitored over 12 months following infusion of study drug and will be registered according to GCP rules.

Results: The project *"ERICONS - Early RITUXIMAB in Childhood Onset Nephrotic Syndrome"*, number 2019/ABM/01/00024 has received funding from the Medical Research Agency, Poland. The study was accepted by regulating agencies and bioethical committees in 2020. The first patient was included in December 2021 and recruitment is planned till June 2023.

Nephrotic syndrome

P3-606 - Plasma oxidative stress levels in children with nephrotic syndrome and their predictive value for steroid sensitivity

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Background: To examine the plasma oxidative stress levels in children with primary nephrotic syndrome (PNS) and whether it can contribute any prediction to the sensitivity of steroid therapy.

Methods: 53 children with PNS and 20 age- and gender-matched healthy controls were enrolled. Patients were divided into two groups: steroid-sensitive (SSNS) group (N=40) and steroid-resistant (SRNS) group (N=13), according to the effect of a standard dose steroid therapy for four weeks. The plasma levels of advanced oxidation protein products (AOPP), malondialdehyde (MDA), and superoxide dismutase (SOD) were tested in controls and patients before and after four weeks of steroid therapy.

Results: Compared with the control group, plasma AOPP and MDA levels of patients were significantly higher; SOD levels were significantly lower. Compared to SSNS and SRNS groups before steroid therapy, plasma AOPP and MDA levels in SRNS were significantly higher, SOD levels were significantly lower (P<0.05). Before glucocorticoid treatment, plasma AOPP levels positively correlated with MDA and negatively correlated with SOD. What's more, urine protein positively correlated with plasma AOPP levels and negatively correlated with SOD levels. AOPP<94.2umol/l, MDA<15.8nmol/l, and SOD>71.9u/ml before steroid therapy showed better predictive value for steroid sensitivity.

Conclusions: The imbalance of oxidative stress in children with PNS behaves with increasing plasma AOPP and MDA levels and decreasing SOD levels. The imbalance is more significant in SRNS than SSNS. The levels of oxidative stress in plasma may predict the sensitivity of steroid therapy in children with PNS.

Miscellaneous (topic not included elsewhere)

P3-607 - P2X receptor activation mediates complement induced injury on endothelial cells

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Introduction: The complement system is central to innate immunity. It consists of over 50 proteins, provides defense against microbes, and mediates inflammatory responses. The final step of complement activation is formation of the membrane attack complex (MAC, C5b-9). Complement over-activation is implicated in the pathophysiology of numerous diseases, yet the mechanisms underlying host cell damage are not fully elucidated.
The P2X receptors, are transmembrane cationic channels gated by adenosine triphosphate (ATP) which are present in the plasma membrane (PM) of most excitable and non-excitable cells. Recently, a link between complement and P2X receptors has been established, showing that inhibition of P2X activation decreases complement mediated cell damage.
Aim: To determine the role of P2X receptors in complement activation on endothelial cells.
Methods: Complement was activated on blood outgrowth endothelial cells (BOECs) using an established protocol, first sensitizing the cells using anti-CD59 antibody followed by treatment with normal human serum. Complement activity was assessed by measuring C5b-9 on BOEC PM via immunofluorescence. Intracellular Ca2+ levels were measured using a fluorescent calcium indicator (Invitrogen). ATP release was measured using a commercial ATP luminescence assay (Promega).
Results: Complement activation caused C5b-9 deposition on BOEC´s PM, as well as Ca2+ influx and ATP release. Cells treated with P2X receptor antagonists, showed a significant decrease in C5b-9 deposition compared to untreated controls. In addition, P2X antagonist treatment significantly ameliorated Ca2+ influx as well as ATP release.
Conclusion: The finding of reduced C5b-9 deposition on BOECs in the presence of P2X receptor antagonists suggests an important functional link between the complement system and purinergic system. While more research is required to fully elucidate the interactions between these critical, ubiquitous biological systems, our results contribute to a better understanding of the consequences of complement activation on endothelial cells and suggest new therapeutic targets for complement associated diseases.

Miscellaneous (topic not included elsewhere)

P3-608 - A Rationale to Replace Age-Based Serum Creatinine (SCr) Reference Ranges with Age-Specific Estimated Creatinine (ECr) values

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Background: Normal SCr concentrations in children increase with age because of increasing muscle mass. SCr based GFR estimation equations, and a 50% increase in SCr above baseline, are commonly used to diagnose chronic kidney disease (CKD) and acute kidney injury (AKI), respectively. The SCr value (normal or flagged) is the most common initial result encountered by physicians. Currently, most clinical laboratories combine normal SCr reference ranges in up to 5-year age group blocks. Such grouping can result in a missed diagnosis of 1) CKD Stage 2 in a child near the younger end of an age group block because of unflagged SCr, or 2) AKI due to unflagged values failing to exceed the upper limit of the reference range, unless an electronic alert has been incorporated in the EHR system.
It is a common practice by researchers to impute missing SCr values from eGFR equations with a presumed GFR of 120 mL/min/1.73m^2. Our objective was to calculate age specific SCr reference ranges for children 2 – 18 years.
Methods: We used CKiD U25 eGFR calculator to calculate ECr for children ages 2 - 18 years by using 3rd percentile for height and GFR of 140 mL/min, and 97th percentile for height and GFR of 90 mL/min for lower and upper SCr limits, respectively. Height values for respective ages were taken from the CDC charts.
Results: The ECr values (for males) are shown in Table. Based on these age specific upper limits of ECr, the diagnosis of CKD stage 2 will not be missed unless the child's height is >97th percentile. Similarly, most cases with AKI will be automatically flagged because of narrow reference ranges.

Table: Age specific ECr values (Males) using CKiD U25 eGFR equation

Age (Yrs)	GFR 140, Ht 3rd percentile		GFR 90, Ht 97th percentile	
	Height 3rd percentile	U25 eCr Lower Limit	Height 97th percentile	U25 eCr Upper Limit
2	79.9	0.21	93	0.37
3	88.4	0.23	103	0.42
4	94.6	0.25	110.5	0.45
5	100.3	0.27	117.8	0.48
6	106.1	0.28	125.1	0.52
7	112	0.30	132.3	0.55
8	117.5	0.32	139.3	0.59
9	122	0.33	145.7	0.62
10	126.7	0.35	151.5	0.64
11	130.8	0.36	157.3	0.68
12	135.7	0.38	163.7	0.71
13	141.7	0.41	171.4	0.77
14	148.5	0.45	178.8	0.84
15	154.6	0.49	184.1	0.91
16	158.9	0.53	187.1	0.96
17	161.3	0.56	188.6	1.02
18	163	0.59	189.5	1.06

Conclusion: We believe that using ECr values will lead to fewer missed cases of CKD or AKI in children, irrespective of age.

Miscellaneous (topic not included elsewhere)

P3-609 - Echogenic Urine on Renal Ultrasound in Paediatric Patients - Implications for Practice

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Background: Echogenic debris on ultrasound is not uncommon in paediatric patients and has previously been linked to increased likelihood of positive urine culture. Our aim is to clarify the connection between

echogenic urine and urinary tract infection within our local population, with intention to develop a clear pathway to improve practice.
Methods: We performed a retrospective database search using terms "echogenic urine", "debris" and "specimen". This identified 74 patients under 16 years with echogenic urine on ultrasound between January and December 2021. We chose to focus on outpatient scans, as those conducted as inpatients were often already known to have infection. Findings were correlated with urine microscopy and culture sent around the time of scanning (+/-3 days). We also looked at electronic patient records for details of urinary symptoms, antibiotic prescriptions or co-morbidities. Sterile pyuria or mixed growth on culture were classed as indeterminate.
Results: 48 (65%) of the scans were conducted on an outpatient basis. 58% of these patients had a urine sample sent. Of these, 21% were positive, 61% negative, and 18% indeterminate. All those with a positive culture were known to have recurrent UTI's, a structural renal abnormality or co-existing constipation.
Discussion: The significance of echogenic urine remains to be established. Not all those presenting had urine sent for culture, which may represent differences in practice, misplaced samples, or where parents have not followed through with requests to provide samples. As our study was retrospective, clinical details were not always available which made symptom correlation less reliable. Despite this, no untreated patients re-presented to the children's assessment unit with UTI. A larger sample with prospective data collection may allow for better clinical correlation, and identification of ways in which to improve practice e.g. ensuring timely collection and follow up of urine samples, particularly for those with co-morbidities.

Miscellaneous (topic not included elsewhere)

P3-611 - Effects of the COVID-19 Pandemic on Adolescent and Caregiver Attitudes Towards Telemedicine Use in Pediatric Nephrology

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[3]*Children's Hospital- London Health Sciences Centre, Paediatrics, London, Canada*
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Background: We compared both adolescent and caregiver attitudes towards telemedicine before and during the COVID-19 pandemic as a crucial determinant of the changing dynamic of virtual care.
Methods: This qualitative research study analyzed transcribed structured telephone interviews with both 11–18-year-old pediatric nephrology patients and their caregivers, and performed a quantitative analysis of patient demographics, disease factors and distance to tertiary center vs. telemedicine center. Data were compared to previous published results with the same study design before the pandemic.
Results: 14 dyads of adolescents with mean age of 15.2±2.1 years and their caregivers were enrolled and had a mean 35±27 of in person visits and 4±3 telemedicine visits at the time of interviews. The median distance to the center was 184.8 km (range 3.9-1214 km). Six dyads lived >100 km away. While the preferred ratio of telemedicine to in-person visits was 2:1 in caregivers, many emphasized that telemedicine is the safer option right now. Interestingly, adolescents preferred more in person visits during the pandemic (1:1 ratio) compared to pre-pandemic (2:1 ratio). Qualitative analysis: *Consultation-specific factors* were more valued during in-person visits, especially by adolescents. Most themes for *Consultation-specific factors* remained the same before and during the pandemic. However, adolescents more often emphasized comfort, communication, and personal connection for in person visits during the pandemic. *Contextual factors* were valued for telemedicine by adolescents and caregivers. Frustration with the technological aspect of telemedicine and adolescents not taking telemedicine seriously, the two main contextual themes pre-pandemic, disappeared during the pandemic. No disadvantages for telemedicine in the contextual factors were identified during the pandemic study.
Conclusions: The COVID-19 pandemic is changing the adolescent expressed attitudes on the transfer to telemedicine for chronic care. Accurately mapping models of care to these attitudes is an essential determinant of effective management and longer-term engagement.

Miscellaneous (topic not included elsewhere)

P3-612 - Analysis of sleep in children with primary nocturnal enuresis

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Objective: To explore the correlation between sleep problems and the severity of enuresis.
Methods: A total of 675 children aged 5-16 years with primary nocturnal enuresis (PNE) who were diagnosed in the enuresis clinic from June 2020 to August 2021 were selected. The clinical data of the patients' urination and defecation, past medical history, living habits, sleep status, disease specific quality of for children with obstructive sleep apnea 18 items survey(OSA-18) and other clinical data were collected. The correlation between the basic situation, sleep status and severity of enuresis in children with PNE was analyzed.
Results: A total of 675 children with PNE were included in the study. There were 330 cases (48.9%) in the severe group. Among 675 children, sleep habits such as being awakened by parents during sleep (79.1%), insufficient sleep (35.1%), and drinking and eating before going to bed (75.6%) were quite common. The total score of the OAS-18 for children in the severe group was higher than that of the mild / moderate group ($P < 0.001$), and each scores in the severe group were higher than in the mild/moderate group ($P < 0.05$). The total score of the OSA-18 was an influencing factor for the severity of enuresis in children, and the higher the score of the OSA-18, the higher the risk of severe nocturnal enuresis ($OR = 1.019$, 95%CI 1.009-1.029, $P < 0.001$). The OSA-18 total score of 114 cases (16.9%) were moderate or severe. There was a statistically significant difference in the severity of enuresis between the groups(P=0.002).
Conclusions: Sleep problems are quite common in children with PNE. It is necessary to pay attention to promote reasonable parenting methods and family lifestyles, actively strengthen life behavior training, improve the quality of sleep, and assess the risk of sleep disordered breathing timely.

Miscellaneous (topic not included elsewhere)

P3-613 - How to measure glomerular filtration rate in multivisceral transplantation?

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The assessment of renal function in patients with non-renal solid organ transplantation is complex as several causes of renal injury are involved. In addition, children with multivisceral transplantation

suffer episodes of hypovolemia, hydroelectrolytic alterations previous to transplantation and have reduced body mass, which causes creatinine glomerular filtration rate (GFR) may be overestimated.
We described the evolution of GFR by creatinine and cystatin C pre- and post-transplantation in patients older than 2 years with a first multivisceral transplantation between 2013 and 2021.
18 patients (11 males/ 7 females), mean age 6.23±4.7 years, diagnosed with short bowel (4 volvulus, 3 necrotizing enterocolitis, 3 tumor disease, 3 pseudoobstructions, 2 hirschprung disease, 3 others) and with multivisceral transplantation (16 with preservation of spleen).
Table 1 shows the GFR, by cystatin C and creatinine at different times of evolution. Only two patients had a decreased GFR prior to transplantation, but at final evolution 80% had alteration of GFR.
3/15 had hypertension prior to transplantation, 1 of them with antihypertensive treatment. After, 5/17 had hypertension and all of them required pharmacological treatment (1-4 drugs). 11 urine tests were analyzed just 2 with significant proteinuria pre-transplantation and in 15 analyzed post-transplantation just 1 had proteinuria. Previous transplantation kidney ultrasound was normal in 12 cases (1 microcysts, 2 echogenicity alteration, 2 megacystic bladder and ureterohydronephrosis, and 1 nephromegaly). Post-transplantation there were no changes in echography.
77.7% of the children required follow-up care with a pediatric nephrologist, 71.5% after transplantation.
Six died during the follow-up period with an mean time after transplantation of 9.8±8.6 months.
The assessment of GFR by creatinine and cystatin C did not predict the risk of renal damage in our patients. While we identified other markers for the early detection of renal failure, in our environment cystatin C is the best marker of renal damage.

	Filler GFR Cystatin C (ml/min/1,73m2)	GFR ≤90 Cystatin C (%)	GFR Schwartz (ml/min/1,73m2)	GFR ≤90 Creatinine (%)	p Value
First GFR	122±36 (31-176)	13,3	134±45 (91-238)	0	0,395
Pre-trasplant GFR	120±29 (61-160)	14	154±39, (92-239)	0	0,033
7 days post-trasplant GFR	70,5±35 (30-166)	78,6	117±96 (25-384)	44	0,075
1 month post-trasplant GFR	57±20 (32-113)	93,3	128±53 (54-242)	25	‹0,0001
6 months post-trasplant GFR	72±19 (37-113)	86,7	130±35 (77-189)	6,7	‹0,0001
Final GFR	73±21 (27-103)	80	109±41 (46-182)	31,3	0,002

Table 1. Evolution of renal function by creatinine and cystatin C

Miscellaneous (topic not included elsewhere)

P3-614 - Gross hematuria ten years review in pediatric emergency department in Brussels

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Context: Gross hematuria is characterized by the presence of a high number of red blood cells in the urine visible to the naked eye. It remains a relatively frequent reason for consultation in pediatrics. The most common causes in children are urinary tract infections but there are potentially severe glomerular or urological causes that require rapid diagnosis and management.
Objective: the purpose of this study is to evaluate: causes, diagnostic approach, also the immediate management of patients admitted to the pediatric emergency department for gross hematuria.
Methods: This is a retrospective monocentric study. We included 179 patients who consulted for gross hematuria in the emergency room of the hospital between December 2007 and December 2017.
Results: The incidence and main causes of gross hematuria in our series are similar to literature data. We found in order of frequency: urinary tract infections (51%), glomerulopathy (11%), stones (3%), trauma (3%), haematological (3%), congenital urologic condition (1%) and toxic (1%). On the other hand 27% of cases remains undiagnosed. It is noted that among the patients weren't of follow-up a considerable number remain undiagnosed. We also observe that the investigations of patients in the emergency room was inharmonious, especially in regards to performing an abdominal ultrasound which was only performed in half of patients. Finally, it is interesting to note that 25% of patients required hospitalization.
Conclusion: Gross hematuria is a symptom that can lead to several renal or urological etiologies, although infectious causes dominate, more serious causes should not be neglected. In our series we find that the diagnostic approach in the emergencies remains heterogeneous and not systematized. Moreover, the lack of follow-up in a large number of patients often left without diagnosis requires a systematization of the management in order to optimize the quality of management of patients with gross hematuria.

Miscellaneous (topic not included elsewhere)

P3-615 - SARS-CoV-2 infection in children with glomerulopathies in Uruguay: clinical features, severity, and risk of relapses.

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Introduction: Coronavirus disease 2019 (COVID-19) is a novel viral disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus. The course of the disease is mild for most affected children with underlying kidney disease, in comparison with adult patients. In Uruguay, official data actualized to February 2022 showed 788.676 confirmed cases; 90.800 of them were children <15 years.
Objectives: The aims were to describe the severity of SARS-CoV-2 infection in children with primary or secondary glomerulopathies and to evaluate the risk of relapses of the underlying disease.
Methods: A retrospective study was performed (from April 1, 2020, to February 15, 2022) of children younger than 15 years infected with SARSCoV-2 previously diagnosed with a chronic glomerulopathy. For inclusion, SARS-CoV-2 polymerase chain reaction result had to be positive. A questionnaire was sent to all the Pediatric Nephrologists of Uruguay. Symptoms, analytical data, previous underlying disease, comorbidities, immunosuppressive (IS) treatment, and evolution data were collected.
Results: 22 children were included; 21/22 had a normal glomerular filtration rate, one had a stage 2 of chronic kidney disease, 17/22 were on complete remission. The course of the disease was mild for 18/22 patients; 5 had no symptoms.

54% had fever, 50% mild respiratory symptoms, and 27% gastrointestinal symptoms. Three patients needed hospitalization, without respiratory support. Two patients had Acute Kidney Injury, one of them (with normal previous kidney function), required dialysis. Three patients had a relapse of nephrotic syndrome, and 3 presented non nephrotic proteinuria with good response to steroids. Only 3 patients had received 2 doses of COVID-19 vaccination.
Conclusions: Children with chronic glomerulopathies and immunosuppression are not at higher risk of severe SARS-CoV-2 infection. Relapses of underlying disease and AKI are possible complications. Given that there are asymptomatic children, the real number of patients is probably much higher.

Demographics, underlying disease and immunosuppression N=22

Male/Female	15/7
Age Median	10(2-14)
Steroid Sensitive Nephrotic Syndrome	8/22
Steroid Resistant Nephrotic Syndrome (FSGS)	3/22
IgA Nephropathy/Vasculitis	6/22
Lupus Nephritis	3/22
IgM Nephropathy	1/22
C1q Nephropathy	1/22
Previous IS drugs:	
Corticosteroids	21/22
Mophetil Mycophenolate	11/22
Cyclosporine	6/22
Cyclophosphamide	6/22
Current IS drugs:	
No IS therapy	7/22
Prednisone	10/22
Mophetil Mycophenolate	6/22
Cyclosporine	5/22
Cyclophosphamide	1/22
Comorbitities:	
Diabetes	1/22
Obesity	2/22

Miscellaneous (topic not included elsewhere)

P3-616 - Comparing fellow and attending pediatric nephrologists' perspectives on palliative care for children with chronic kidney disease: a cross-sectional survey

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Background: Integration of palliative care (PC) into routine nephrology practice offers the opportunity to promote flourishing and lessen burdens experienced by children with chronic kidney disease (CKD) and their families. Adult nephrologists report feeling unprepared to deliver PC. The analogous perspective of pediatric nephrologists and how it may evolve over time is unknown. We sought to compare pediatric nephrology fellows and attendings' experiences, knowledge, and confidence in providing primary PC.
Methods: A cross-sectional web-based survey was administered to pediatric nephrology fellows and attendings through professional group listservs in summer 2021. The survey was adapted from the Provider Survey about Palliative Care for Children with Heart Disease and pretested by PC physicians and pediatric nephrologists; queries included institutional and personal PC experience, training and education, and physician confidence in PC delivery. Data were summarized descriptively. Chi-squared tests were used to assess differences in responses of fellows and attendings.
Results: 32 pediatric nephrology fellows and 65 attending nephrologists responded. Both fellows and attendings noted challenges addressing physical and psychosocial symptoms of children with CKD, and most desired to receive additional training in these domains. Fellows and attendings similarly lacked confidence addressing pain; only 24% and 37% of attendings and fellows, respectively, felt confident managing pain. Likewise, only 28% and 24% of attendings and fellows, respectively, felt confident addressing the psychological distress of a child with CKD. Significant differences were seen, however, with challenging communication delivery. 81% of attendings and 31% of fellows indicated that they felt confident discussing goals of care of the family of a child with CKD ($p<0.01$).
Conclusion: While confidence in challenging communication delivery among pediatric nephrologists may improve over time, confidence in addressing physical and psychosocial symptoms remains low. Pediatric nephrology fellows and attendings indicate a need and desire for additional primary PC training.

Miscellaneous (topic not included elsewhere)

P3-617 - Therapeutic Plasma Exchange (TPE) in Pediatric Patients with Kidney Disorders: An 8-Year Experience from a Tertiary Care Center

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Background: TPE is widely used in kidney diseases. American Society for Apheresis (ASFA) provides clinical guidelines in adults; however, little has been described in children. We aimed to study indications, complications & outcomes of TPE in various pediatric kidney diseases.
Subjects & methods: A retrospective review of pediatric cases received TPE for kidney diseases over 8 years duration.
Results: A total of 1979 TPE sessions were performed on 118 patients (55.1% males & 44.91% females) with age of 7.6 ±4.4 years. As per ASFA guidelines 77.1% & 22.9% of cases were categories I & III & 0.85%, 52.54% & 46.61% of patients were grades 1A, 1B & 2C respectively. Indications for TPE included aHUS (45.7%), active antibody mediated rejection (34.7%), DSA desensitization (17.7%), FSGS post transplantation (16.1%), ANCA (+ve)-RPGN (0.8%) & HSP- RPGN (0.8%) of the cases. Centrifugation technique with citrate as anticoagulant & membrane separation technique with heparin were used in 93.2% & 6.8% of the sessions respectively. In all sessions, Albumin & fresh frozen plasma were used together as a replacement therapy. Complications were reported in 9 patients (7.6%), included non-manifest hypocalcemia, hypotension & hypokalemia, clotted extracorporeal circuit & filter rupture in 2.5%, 1.7%, 0.8%, 1.7% & 0.8% of cases respectively. Response to TPE was complete in 71.2%, partial in 20.3% & no response in 8.5% of patients. We found statistical evidence of significant strong association between patients' age & RRT need with disease outcome ($p= 0.003$ & 0.001 respectively), with highest complete recovery among age group of 5-10 years (90%) & among group

of patients who didn't need kidney replacement therapy (77%). We had 1 TPE related death (0.8%) due to clotted circuit.
Conclusions: TPE is a relatively well-tolerated useful primary & adjunct therapy in children with renal diseases, where benefits must be balanced with risks.
Keywords: ASFA, Outcomes, RRT, TPE

Age, Sex, Diagnosis, ASFA Category & Grade, RRT, Disease Outcome, TPE Sessions

Patients (n=118 patients, Age = 7.686 ± 4.44 years)		
Age Groups	0-5 years	40 (33.9%)
	>5 – 10 years	40 (33.9%)
	>10 years	38 (32.2%)
Sex	Male	65 (55.1%)
	Female	53 (44.9%)
Diagnosis	aHUS	54 (45.8%)
	PKTx FSGS	19 (16.1%)
	Active AMR	41 (34.7%)
	Pre-kidney Tx desensitization	2 (1.7%)
	RPGN ANCA	1 (0.8%)
	RPGN HSP	1 (0.8%)
ASFA Category	I	91 (77.1%)
	III	27 (22.9%)
ASFA Grade	1A	1 (0.85%)
	1B	62 (52.54%)
	2C	55 (46.61%)
Renal Replacement Therapy (RRT)	No	87 (73.7%)
	Yes	31 (26.3%)
Disease Outcome	Complete Remission (CR)	84 (71.2%)
	Partial Remission (PR)	24 (20.3%)
	No Response (NR)	10 (8.5%)
Disease Outcome in Relation to Age Groups	0-5 Years	CR: 25 (62.5%)
		PR: 8 (20%)
		NR: 7 (17.5%)
	>5-10 Year	CR: 36 (90%)
		PR: 3 (7.5%)
		NR: 1 (2.5%)
	>10 Years	CR: 23 (60.5%)
		PR: 13 (34.2%)
		NR: 2 (5.3%)
Disease Outcome in Relation to RRT	Group without RRT	CR: 67 (77%)
		PR: 17 (19.55%)
		NR: 3 (3.45%)
	Group Needed RRT	CR: 17 (54.8%)
		PR: 7 (22.6%)
		NR: 7 (22.6%)
TPE Sessions (n=1979 sessions)		
Technique	Centrifugation	1845 (93.2%)
	Membrane Plasma Separation	134 (6.8%)
Anticoagulant	Citrate	1845 (93.2%)
	Heparin	134 (6.8%)
Replacement Fluid	Albumin + Fresh Frozen Plasma	1979 (100%)

Miscellaneous (topic not included elsewhere)

P3-618 - Low seroprevalence of COVID-19 in UK children on renal replacement therapy – results from the ISpy COVID study.

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Introduction: COVID-19 was officially declared a pandemic by the WHO on 11 March 2020 as the novel SARS-CoV-2 virus rapidly spread globally. We established the ISpy study to investigate the seroprevalence of SARS-CoV-2 in paediatric patients on renal replacement therapy (RRT) in the United Kingdom.
Methods: Samples were obtained opportunistically using excess sera from patients during outpatient visits or haemodialysis sessions (prospective), and retrospective samples from CountOnMe home testing, where available. Two large paediatric centres contributed samples. Antibodies were detected against spike and nucleocapsid antigens using a custom ELISA. Age-matched negative controls were used to define the threshold for positivity.
Results: In total, 520 sera from 152 patients (17 peritoneal dialysis, 18 haemodialysis, 117 transplantation) were analysed cross-sectionally by month [Figure1]. No SARS-CoV-2 antibodies were detected in 2020 when lockdown and enhanced social distancing measures were in place. Thereafter, the proportion of positive samples increased to a peak of 32% (12/37) in August 2021. Antibodies were preceded by laboratory-confirmed Covid-19 infection in 7/32 (22%) patients and known COVID vaccine administration (from February 2021) in 9/32 (28%). Median antibody levels were 0.8 units (IQR 0.5-1.4). Three patients had positive PCR without detectable antibodies. Antibodies were detected in all patients who had the first vaccine dose, though in 6/9 patients, antibody levels were low (<1). Antibody levels were comparable across patient ages and mode of RRT.
Summary: The seroprevalence due to SARS-CoV-2 infection was low though we could rule out patients who had COVID-19 without detectable antibodies. Conversely, antibody testing revealed additional cases without known symptomatic infection. Antibody responses to the COVID vaccine warrant further investigation.

Figure1: Antibody responses to Sars-CoV-2, tested monthly (cross-sectional). Nott'm: Nottingham University Hospital, Glasgow: Royal Hospital for Children, Glasgow

Miscellaneous (topic not included elsewhere)

P3-619 - Renal complications and short- term outcome in Bilateral Wilms Tumour – A Case series

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Although accounting for only 4% to 7% of all Wilms tumours (WT), bilateral Wilms tumours (BWT) pose a special challenge in management because of the conflicting goals of removing the tumour completely for cure while preserving as much renal tissue as possible for a favourable renal outcome. We undertook this study in 15 children (10 girls,5 boys) who underwent surgery for BWT over a 4-year period. The median age at diagnosis was 22.2 months (9 to 52 months). 13 had synchronous and 2 had metachronous tumours. 7 underwent radical nephrectomy on one side with nephron sparing surgery (NSS) on the other, 6 had NSS on both kidneys, 1 had bilateral nephrectomy.

Preoperatively, 1 patient had 2 episodes of acute kidney injury, first due to contrast administration requiring haemodialysis and second due to ureteric obstruction that resolved with conservative management. 1 expired due to haemorrhagic tumour rupture before nephrectomy. Baseline creatinine was normal in others; 9 were hypertensive.
Post operatively, 13/14 showed rising creatinine within 72 hours, with more than 3-fold higher than baseline in 6 (40%), 2.0-2.9 times higher in 5 (33%), 1.5-1.9 times higher in 1(6%), 1 was anephric. All had hypoalbuminemia, 8 (53%) with 20-50% drop from preoperative values. Of these, 4(50%) had persistent drain fluid leak (1 urinary leak), lasting more than a week post-surgery.
At discharge, estimated GFR was greater than 90 ml/min/1.73m ^{2} in 8(61%), between 60-89 ml/min/1.73m ^{2} in 5(38%) and anuria in 1 on maintenance HD. 13 were hypertensive, controlled on medications. 13(87%) survived. 2 died, one due to pre-operative haemorrhagic tumour rupture and another on maintenance HD in another city.
With multidisciplinary care in dedicated centres, BWT has a good short-term outcome with 87% survival and only 1 requiring long term dialysis. However, long term outcome needs a close watch.

Miscellaneous (topic not included elsewhere)

P3-620 - #IPNAJC, a Twitter-based IPNA Journal Club: a Bilingual Medical Education Tool

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Background: The International Pediatric Nephrology Association (IPNA) fosters the international exchange of knowledge without barriers. Aligned with this goal, the IPNA social media (SoMe) sub-committee initiated a free, quarterly Pediatric Nephrology journal club (#IPNAJC) in July 2021, modeled after #NephJC, a well-regarded Nephrology journal club on Twitter.
Aim: To describe the anatomy of #IPNAJC.
Methods/Results: The SoMe sub-committee selects one or two recently published articles highly relevant to the pediatric nephrology field. The team prepares a summary and a few corresponding visual abstracts, which are published on the IPNAJC website (https://theipna.org/journalclub/) and distributed to IPNA members via email and on Twitter a few days prior to #IPNAJC.
Two separate live, one-hour discussions are scheduled to coincide with times that are maximally convenient across major international time zones. The team creates a chat script to organize and guide the discussion and posts content from the official Twitter account, @IPNAJC, using the hashtag #IPNAJC. Participants can join the discussion by searching for #IPNAJC. An infographic (Figure 1a) and a video (pinned to the @IPNAJC account) to educate new participants and a code of conduct infographic (Figure 1b) to promote camaraderie and professionalism, are distributed before and during the chat.

Figure 1a

Figure 1b

To enrich the conversation, the article's authors and relevant content experts are invited to participate. In addition, #IPNAJC distributes free open access medical education (FOAMed) materials, including visual abstracts, online poll questions, and a synchronous online chat in Spanish. After the event, the discussion is curated in the "#IPNAJC wrap-up" and emailed to IPNA members 1-2 weeks later.
Conclusions: #IPNAJC is a FOAMed tool that offers a bilingual forum for international discussion and critical review of relevant literature in pediatric nephrology. Future plans include exploring other platforms to hold #IPNAJC, engaging a wider audience and offering discussion in more languages.

Miscellaneous (topic not included elsewhere)

P3-622 - Heterogenous antibody and T-cell responses to SARS-CoV-2 mRNA vaccines among immunocompromised young people with kidney disease

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Introduction: This study aimed to evaluate the humoral and cellular responses to SARS-CoV-2 mRNA vaccines in immunocompromised young people with kidney disease as their response is largely uncharacterized and vaccination recommendations have been extrapolated from adult practice.

Methods: Immunocompromised patients (on corticosteroids, antimetabolites, calcineurin inhibitors, or with end-stage kidney disease) between 12-25 years old with kidney transplant, kidney failure, idiopathic nephrotic syndrome, IgA nephropathy/vasculitis, or systemic lupus erythematosus, were prospectively recruited with controls. Antibodies and T-cell responses (via interferon-gamma release assay) against the SARS-CoV-2 spike protein were quantified after 2 standard doses of SARS-CoV-2 mRNA vaccines.
Results: 54 immunocompromised patients and 20 controls were recruited. 32 (59%) patients had anti-spike protein titers >250U/ml, compared to 20 (100%) controls (p=0.0003). Patients had reduced pan T-cell [-0.14±0.11 vs 0.24±0.09 logIU/ml, p=0.044] and CD4+ T-cell responses [-0.55±0.15 vs -0.003±0.09 logIU/ml, p=0.038] to spike protein compared to controls. There were differences in the proportion of antibody (p=0.014) and CD4+ T-cell responders (p=0.002) between disease categories (Table 1). On multivariable analysis, corticosteroids were associated with reduced humoral [OR=0.064 (95% CI:0.008-0.533), p=0.01] and to a lesser extent cellular responses, while calcineurin inhibitors were associated with reduced pan T-cell [-0.563 (95% CI: -1.106- -0.021) logIU/ml, p=0.042] and CD4+ T-cell responses [-0.903 (95% CI: -1.653-0.153) logIU/ml, p=0.019]. Interestingly, even after adjusting for immunosuppression through stratified analysis of patients on anti-metabolite monotherapy (n=28), there remained differences in pan T-cell (p=0.042) and CD4+ T-cells (p=0.045) responses between disease categories.
Conclusions: Immunocompromised young people with kidney disease display attenuated responses to vaccination but there are significant differences between disease subgroups. This is partially due to differing immunosuppressant use, but is likely contributed by immune dysregulation inherent in these conditions. Patients with certain immune-mediated kidney diseases not on immunosuppression, e.g. IgA nephropathy, may benefit from a third primary mRNA vaccine dose.

	Controls	All immuno-suppressed	Kidney transplant	End-stage kidney disease	Nephrotic syndrome	IgA nephropathy/ vasculitis	Systemic lupus erythematosus
n	20	54	12	11	12	7	12
Age (years)	17.10±0.66	18.19±0.47	18.55±1.03	17.82±1.12	17.43±0.99	18.88±1.51	18.50±0.93
Female (%)	7 (35)	27 (50)	6 (50)	1 (9)	4 (33)	5 (71)	11 (92)
Pfizer (%)	18 (90)	54 (100)	12 (100)	11 (100)	12 (100)	7 (100)	12 (100)
Days between Doses	31.7±1.75	34.56±1.14	39.33±1.48	41.09±2.00	33.25±2.07	30.71±4.3	27.33±1.17
Days after Dose 2	38.75±3.22	37.26±1.59	37.67±3.19	38.82±4.12	36.08±3.38	34.86±3.53	38.00±3.75
Steroids (%)	0 (0)	21 (39)***	12 (100)	0 (0)	1 (8)	4 (58)	4 (33)
Anti-metabolites (%)	0 (0)	40 (74)***	10 (83)	0 (0)	11 (92)	7 (100)	12 (100)
Calcineurin inhibitors (%)	0 (0)	18 (33)**	12 (100)	0 (0)	5 (42)	1 (14)	0 (0)
Anti-S >250 U/ml (%)	20 (100)	32 (59)***	6 (50)	11 (100)	5 (42)	2 (29)	8 (67)
Anti-S >100 U/ml (%)	20 (100)	36 (67)**	9 (75)	11 (100)	5 (42)	2 (29)	9 (75)
Anti-S >0.8 U/ml (%)	20 (100)	47 (87)	10 (83)	11 (100)	10 (83)	5 (71)	11 (92)
Pan T-cell IFNγ response (log IU/ml)	0.24±0.09	-0.14±0.11*	-0.76±0.29	0.19±0.19	-0.28±0.19	-0.12±0.21	0.30±0.19
CD4+ T-cell IFNγ response (log IU/ml)	-0.00±0.09	-0.55±0.15*	-1.36±0.36	-0.05±0.19	-0.76±0.36	-0.40±0.22	-0.07±0.30

Table 1: Baseline characteristics, immunosuppressive medication use, humoral and cellular vaccine responses in controls and immunocompromised young people with kidney diseases. Frequency data are given as n (%). Summary data are given as mean ± SEM. *, **, *** refers to significant differences between controls and the immunocompromised cohort with p < 0.05, 0.01 and 0.001

Miscellaneous (topic not included elsewhere)

P3-623 - Neutralizing antibodies after 3 doses of mRNA COVID-19 vaccine in adolescents with kidney disease

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Background: The immunogenicity of a two-dose mRNA COVID-19 vaccine regimen is suboptimal in adolescent with kidney diseases. We examine the immunogenicity and safety of a three-dose COVID-19 vaccine regimen in this population against Omicron BA.1, which is causing the current global pandemic.
Methods: A prospective longitudinal study was performed in 20 COVID-19 naïve adolescent patients (12-18 years) with kidney diseases. Patients received 2 or 3 doses of BNT162b2 COVID-19 vaccine administered at 0 weeks, 3 weeks, and 7-33 weeks. We evaluated the levels of Omicron BA.1 neutralizing antibodies by surrogate virus neutralization test after the second and third doses. Adverse reactions and events were documented.
Results: A total of 20 patients [M:F 9:11; age 12-18 years (median 16)] were included. Six patients were on dialysis, 6 patients received a kidney transplant and 8 patients had glomerulonephritis and were on immunosuppressive agents. Compared with healthy age-matched controls, fewer tested patients demonstrated a positive Omicron-neutralizing antibody response after the second dose of vaccine (21% vs 83%, p<0.0001). However, there was a significant increase in the Omicron-neutralizing antibody seropositivity after the third vaccine (79% vs 21%, p=0.002). Most non-responders after 3 doses were on immunosuppressants post-transplant. Adverse reactions were mostly mild.
Conclusion: Our results show that antibody response to Omicron BA.1 in uninfected adolescents with kidney diseases is lower than healthy adolescents. Antibody response is demonstrated with three doses of vaccines in most patients with mild adverse reactions. A three-dose COVID-19 vaccine regimen should be considered in this patient population to ensure robust antibody response to prevent morbidity and mortality from COVID. Post-immunization T cell responses and the potential need of a fourth dose of COVID-19 vaccine are being evaluated.

Miscellaneous (topic not included elsewhere)

P3-624 - Entrustable professional activities as an assessment and educational tool in pediatric nephrology

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Background and aim: The entrustable professional activity (EPA) is a construct that allows faculty to assess development of trainees and practitioners and also make competency-based decisions on level of supervision required by trainees. In the US, the American Board of Pediatrics spearheaded development of discipline-specific and general EPAs. 4 pediatric nephrology (PN) specific EPA and 7 general pediatric subspecialty EPAs are now available for use. To better understand their potential use, we asked US PN training program directors to define what levels of PN specific EPAs they would require for graduation from fellowship and to practice independently.
Method: 4 PN specific EPAs [Care of children with 1) acute and 2) chronic kidney disorders; 3) ESKD/transplant and 4) nephrology procedures] were presented and 44 of the 46 program directors in the US responded to a Subspecialty Pediatric Investigators Network survey asking their minimum levels of each EPA expected to achieve by graduation, expected for independent practice and to require for graduation.

Results: Median values for all 4 EPAs expected to achieve by graduation and expected for independent practice was level 4; there was more variation in the minimum EPA levels PDs would require for graduation.

Table: Percentage PDs who would require level 4 or higher for graduation

EPA	% who would require ≥4 for graduation
1 – acute care	57
2 – chronic care	73
3 – ESKD/transplant	75
4 – nephrology procedures	70

Conclusion: The ABP Pediatric Nephrology EPAs can be a useful construct for assessing entrustment, competence and readiness for independent practice for PN trainees throughout the international community.

Miscellaneous (topic not included elsewhere)

P3-625 - Spectrum of renal histopathology in a tertiary care center over 15 years

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Aim: to study the various renal histopathological lesions associated with kidney disease in children aged 0 to 18 years at a tertiary care center.
Method: Retrospective data collection of renal histopathology reports spanning over last 15 years (from January 2007 to January 2022) was done at Jehangir Hospital and Research Centre, Pune, India
Results: Total of 162 biopsies, 73 were biopsied for nephrotic syndrome (either for steroid resistance or before starting calcineurin inhibitors) of which,
MCD accounted for 40/73 (61%),
MCD (Minimal change disease only)-13/73,
MCD with mild mesangial hypercellularity-31/73,
FSGS (Focal Segmental Glomerulosclerosis)-24/73 (32%) and
Congenital NS (CNS) – 5/73 (7%).
The rest 83/162 showed the following glomerular lesions -
IgA Nephropathy – 23
Crescentic GN – 11
IRGN (Infection related GN) – 8
Lupus Nephritis - 9
MN (Membranous Nephropathy) – 4
Acute tubulo-interstitial nephritis – 6
HUS (Hemolytic Uremic Syndrome) – 5
ATN (Acute Tubular Necrosis) – 4
Chronic GN – 3
IgAV(IgA Vasculitis) nephritis – 3
C3 Glomerulopathy – 3 [2 – C3 GN, 1 – DDD (Dense Deposit Disease)]
Alports' syndrome – 1 (confirmed by EM and genetics), histologically showing FSGS
AAV (ANCA Associated Vasculitis) - 2
GWP (Granulomatosis with Polyangiitis) i.e Wegener's granulomatosis - 1
Out of 6 transplant biopsies – 2 showed evidence of tacrolimus toxicity, 1 showed severe ABMR (Antibody mediated rejection) with glomerulitis, tubulitis, vasculitis and a positive C4d staining and 3 showed nonspecific tubular damage (ATN).
Conclusion: Renal histopathology - light microscopy and immunofluorescence both could suffice in establishing a definitive diagnosis, except a few cases where EM (Electron Microscopy) and genetic evaluation helped to elucidate the pathology.

Miscellaneous (topic not included elsewhere)

P3-626 - Downstream signaling of Angiotensin II type 1 receptors responsible for mammalian nephrogenesis

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Angiotensin II (AngII) is important in mammalian early postnatal kidney development. The downstream signaling pathway of the AngII type1 receptor originates from G proteins and β-arrestins. However, the specific role of each pathway in nephrogenesis is not known.
Ang II receptor blocker (ARB) inhibits both the pathways and β-arrestin bias agonist (BBA) inhibits the G protein but activates the β-arrestin pathway. We investigated how the two pathways affect renal development in juvenile mice.
Wild-type BALB c mice subcutaneously received ARB, candesartan (3 mg/kg/day), the BBA, TRV027 (3 mg/kg/day), or saline daily from the postnatal day 1 (P1) to P15. Then, their blood and kidneys were collected after their euthanasia for analysis of renal function and plasma electrolyte concentrations and renal histology with periodic acid Schiff staining, respectively.
The survival rates at P15 were 67, 100, and 100% in ARB, BBA, and saline groups, respectively. Blood tests showed significant renal dysfunction in the ARB group, with significantly elevated concentrations of potassium and inorganic phosphorus. Renal pathology showed a decreased in the glomerular number, cortical thinning, thickened vascular wall mainly in interlobular arteries, and disorganized cell arrangement of vascular smooth muscles. However, these abnormalities were not observed in BBA or saline groups.
These observations indicate that β-arrestin pathway that is differentially regulated by ARB and BBA is responsible for the postrenal kidney development.

Miscellaneous (topic not included elsewhere)

P3-627 - Renal Function status in children with Acute Lymphoblastic Leukemia at diagnosis and after 3 months at end of induction.

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Background: Acute Lymphoblastic Leukemia(ALL) is the commonest malignancy of childhood, accounting for 30% of all paediatric cancer. Kidney is the most common extra-reticular and extra-hematopoietic organ invaded by leukemia. It can occur by leukemic infiltration, metabolic abnormalities caused by chemotherapy, nephrotoxic medications, and sepsis. Derangement of renal function may occur in form of electrolyte imbalance, alteration in serum, urinary and imaging parameters. Besides very few studies currently available, much less is known about follow-up renal function status in these children.
Aims & Objectives: To determine renal function status in children of Acute lymphoblastic Leukemia at diagnosis and after remission at 3 months and correlating renal functions with staging and treatment of leukemia.

Method: Prospective cohort study in sixty children newly diagnosed with ALL. Staging and risk stratification was done in all children and standard management protocol followed. Renal function tests(Complete haemogram, peripheral smear, blood urea, Serum creatinine, Serum sodium, Serum potassium, Serum calcium, Serum phosphate, Serum ALP, Serum uric acid, Venous blood gas, Urine R/M including specific gravity, spot urine calcium/creatinine ratio, FENa(fractional excretion of sodium), Ultrasound KUB with doppler were done at start and repeated after 3 months of diagnosis (end of induction therapy).
Results: Out of 71 children enrolled, finally 60 patients completed the study. Majority of participants 78.3%(47) were B-Cell ALL and 21.7%(13) of the participants were T-Cell ALL. Maximum number of study subjects 85.0%(51) of were of High Risk disease. On comparing serum Biochemical and Urinary parameters (n= 60) at baseline and 3 months there was statistically significant difference in serum potassium (p=0.001), serum phosphate (p <0.001), Serum Uric acid (p= 0.018), urine creatinine (p= 0.005), spot calcium to creatinine ratio (p< 0.001) and FENa.
Conclusion: Renal functions are affected significantly in children with ALL and need careful monitoring.

Miscellaneous (topic not included elsewhere)

P3-628 - Entrustable professional activities to pediatric nephrologist trainees

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Introduction: Entrustable Professional Activities (EPAs) provide a framework to make judgments of trainees' abilities in postgraduate medical education. Pediatric nephrology residents need continued development of clinical and nonclinical skills, underscoring a need for continued assessment and mentoring. Our objective was to develop reliable professional activities for pediatric nephrology residents at the Pediatric Nephrology Unit of the Santa Casa de Belo Horizonte Hospital, in Belo Horizonte, MG, Brazil.
Methods: The content of these EPAs was developed by the hospital's pediatric nephrologists and adult nephrologists, based on current literature and the knowledge required of pediatric nephrologists in clinical practice, and categorized this knowledge into content domains and subdomains. Competency domains included: communication, collaboration, leadership, social responsibility, continuing education, professionalism, and technical excellence. The supervisory scale for EPAs would be: 1) Reliable to observe only; 2) Reliable to perform with direct supervision and training; 3) Reliable to perform with indirect supervision for most simple cases and some complex cases; 4) Reliable to perform with indirect supervision, but may require discussion for some complex cases; and 5) Reliable to perform unattended.
Results: The EPAs defined were: 1) Clinical care of pediatric patients with chronic kidney disease on hemodialysis; 2) Clinical care of pediatric patients with chronic kidney disease on peritoneal dialysis; 3) Clinical care of hypertensive pediatric patients or patients with non-dialysis kidney disease; 4) Clinical care of the pediatric patient with prenatal renal anomalies; 5) Nephrological care for critically ill pediatric patients; 6) Clinical consultation in pediatric nephrology; 7) General approach to the pediatric kidney transplant process; 8) Health education; 9) Transition from the pediatric patient with kidney disease to the adult nephrologist.
Conclusion: We do believe that EPAs are the path to proper and reliable certification of all actions by pediatric nephrology residents, as well as to the development of their education in pediatric nephrology.

Miscellaneous (topic not included elsewhere)

P3-629 - Henoch-Schönlein Purpura (HSP) – What can we learn from Biomedical and Clinical Anatomy Practice on this Multidisciplinary Disease?

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Background: Henoch-Schönlein Purpura (HSP) is the most common vasculitis in children, characterized by triad of symptoms: 1) palpable purpura without thrombocytopenia, 2) abdominal pain, and 3) arthritis. Renal involvement also often occurs in children with HSP. HSP is the most common vasculitis in children, occurring in 8 to 20.4 per 100,000 children per year.
Epidemiology: HSP usually occurs in children aged between 2-10 years, with 50% of all cases occurred in children aged <5 years, mostly in children aged 4-6 years and occurs more frequently in male. Although it is generally a self-limiting condition, HSP can cause renal manifestations with various incidences. The guidelines and treatment for managing care in HSP patients ranges between centres.
Aims: 1) To provide practical understanding of Henoch-Schonlein Purpura (HSP), 2) Highlight the importance of multidisciplinary laboratory practice for patients with HSP, and 3) Highlight what laboratory practices could be enhanced to support the development of HSP guidelines.
Practice: HSP is a multi-specialty disease wherein a patient's care plan will have laboratory involvement from a variety of disciplines. Laboratory investigations suggest that HSP is not a self-limited disease.
Research Stance: A retrospective study of 141 patients with HSP, demonstrated that abdominal pain was not related to HSP Nephritis (HSPN). However, 45% of the patients were complicated with obesity and 29.8% of them had a long disease course. Multidisciplinary laboratory perspectives are paramount in disease follow-up.
Discussion: Future biomedical/ laboratory practices can help tighter clinical decision-making in the care of young people with HSP. More case and longitudinal studies would be helpful to understand whether patients would benefit different care plan options.
Conclusion: Certainly, well-designed, and conventionally reported studies in histology, microbiology and haematology laboratory collaborations are important to identify HSP disease development and progression.
Keywords: Henoch-Schönlein Purpura (HSP), Haematology, Anatomy, Histology, Microbiology, Renal

Miscellaneous (topic not included elsewhere)

P3-630 - Initial kidney damage in a child with acute lymphoblastic leukemia

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Introduction: Kidney damage in leukemia, a more common lymphoblastic origin that occurs in children in 80% compared with adults, develops as a result, of leukemic infiltration of the renal parenchyma, and metabolic personal disorders - increased levels of uric acid,

calcium and lysozyme in the urine. In case of leukemic infiltration, it is characterized by bilateral kidney damage. Lymphoma of kidney origin is extremely rare, occurs in such patients.

Case: A 3 year-old girl was admitted to our hospital with complaints of fever, weakness, shortness of breath and tachycardia. Body weight decreased for 3 kg per month. At the time of examination, the patient was lethargic, with temperature 37.2, BP 90/60mm/Hg, SpO2 89%, an increase in submandibular, cervical and inguinal lymph nodes. Pronounced hepatosplenomegaly, nephromegaly determined by palpation. Initial laboratory test data: Hemoglobin 61 g/l, leukocytes 7.8 10*9u/L, neutrophils 2%, platelets 234 10*3/uL. Creatinine 45.1mkmol/l, Urea 2.9mmol/l, LDH 616 U/L, Potassium 5.02mmol/l. Kidney ultrasound data: right - 102-50mm, cortical thickness 6.0-9.0 mm, left - 100-54cm, cortical thickness 7.0-11.0mm, enlarged, hyper-echoic structure. Urinalysis were as follows: urine occult blood (-), urine protein (-), urine RBC 0-2/ HPF. PET scan revealed lymphoproliferative process. The patient underwent bone marrow biopsy and the result showed acute lymphoblastic leukemia, B-II variant with CD13 co-expression. She was transferred to hemato-oncology department, and started standard chemotherapy. Her kidney function was recovered.

Conclusion: This case shows kidney damage with impaired function at the beginning of the lymphoproliferative process, which greatly complicates the timely diagnosis of a malignant disease. Our clinical case warns of the importance of differential diagnosis of renal pathology with various other diseases that may be primary, including lymphoproliferative processes. For differential diagnosis, PET and bone marrow puncture may be necessary, especially if there are changes in indirect indicators of oncological diseases.

Miscellaneous (topic not included elsewhere)

P3-631 - Febrile urinary tract infections in children in Luxembourg: evolution over time of bacterial ecology and antibiotic resistance

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Background: Febrile urinary tract infections (UTI) are common in children. Management of febrile UTI should take into account morbidity, but also health costs and antibiotic resistance. Here we aimed at analyzing the evolution over time of bacterial ecology and antibiotic resistance in pediatric febrile UTI in Luxembourg, a country particularly representative of the European population.

Methods: We performed a retrospective study of medical and laboratory files of 465 pediatric patients who presented 519 confirmed episodes of febrile UTI, treated in 2014-2015 and 2019-2020 at the National Pediatric Reference Hospital of Luxembourg.

Inclusion criteria were based on age (1 month to 17 years), clinical symptoms (temperature above 38.5°C or below 36.0°C, icterus and/or vomiting in newborns), and lab results (urine leucocytes above 10/mm3, bacterial CFU above 1000, 10 000, or 50 000 per ml according to urine collection means, respectively sus-pubic catheter, urinary catheter or mid-stream). Exclusion criteria were patients lost to follow-up, incomplete documentation, or recent bacterial infection.

Results: Patients' demographic and clinical characteristics are shown in Figure 1A, and were comparable over time.

The most frequent pathogen found on urine cultures was *E. coli* (94.9% in 2014-2015, 88.2% in 2019-2020). The distribution of other pathogens is shown in Figure 1B. The number of febrile UTI caused by *K. pneumoniae* significantly increased over time.

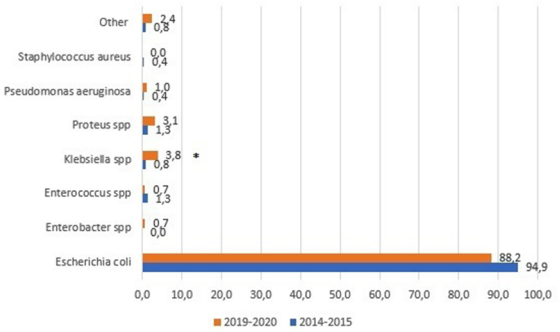
Prevalence of antibiotic resistance for commonly prescribed antibiotics for *E. coli* is described in Figure 1C. Resistance to amoxicillin – clavulanic acid significantly increased over time.

Prevalence of extended-spectrum β-lactamase-producing *E. coli* (ESBL) was 5.3% in 2014-2015 versus 2.7% in 2019-2020.

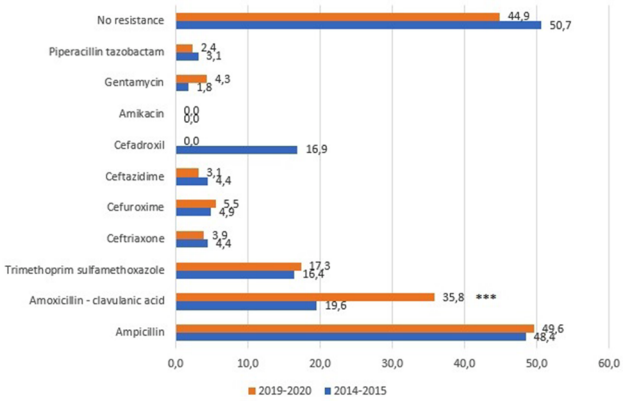
Conclusion: A major increase in amoxicillin – clavulanic acid resistance of *E. coli* was observed over the past 6 years. Prevalence of ESBL remains low; no cases of carbapenem resistant *E. coli* were detected. These results emphasize that antibiotic resistance remains a major issue in pediatric UTI.

Total number of patients	465
Total number of UTI episodes	519
Patients with multiple UTI episodes (%)	8,6
Number of girls - sex ratio G/B	315 - 2,1
Mean age (months) - SD	21,2 - 2,24
Mean weight (kg) - SD	10,21 - 7,008
Mean height (cm) - SD	73,85 - 21,17
Duration of hospitalization (days) - SD	3,067 - 2,24
CAKUT patients (%)	13,5
CAKUT patients in patients with multiple UTI episodes (%)	52,5
Antibioprophylaxis at time of UTI episode (%)	1,54
Infectious complications (%)	3,47

1.A Patients' demographic and clinical characteristics



1.B Evolution of pathogens causing febrile UTI in children over time



1.C Evolution of E. coli antibiotic resistance over time

Miscellaneous (topic not included elsewhere)

P3-632 - Contribution of renal ultrasound to the diagnosis and prognosis of febrile urinary tract infections in children

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Background: The contribution of renal ultrasound (RUS) during febrile urinary tract infections (UTI) remains debatable, in particular in non-complicated *E. coli* infections, or during a first episode of UTI. Here we aimed at analyzing the impact of RUS on diagnosis and prognosis in pediatric febrile UTI in Luxembourg, a country particularly representative of the European population.
Methods: We performed a retrospective study of medical and laboratory files of 465 pediatric patients who presented 519 confirmed episodes of febrile UTI, treated in 2014-2015 and 2019-2020 at the National Pediatric Reference Hospital of Luxembourg.
Control patients were also included; they presented a non-recurrent febrile episode with negative urine cultures.
Results: Patients' demographic and clinical characteristics were comparable between groups.
The performance metrics of pyelitis, nephritis and perinephric fat infiltration are shown in Table 1.

	Pyelitis	Nephritis	Perinephric fat infiltration
Sensitivity (95% CI)	55,30 (50,90 - 59,63)	47,40 (43,03 - 51,80)	13,49 (10,67 - 16,71)
Specificity (95% CI)	53,85 (33,37 - 73,41)	73,08 (52,21 - 88,43)	92,31 (74,87 - 99,05)
Accuracy (95% CI)	55,01 (50,72 - 59,24)	52,53 (48,25 - 56,80)	29,25 (25,46 - 33,27)
Positive predictive value (95% CI) *	82,74 (75,85 - 87,97)	87,57 (78,79 - 93,03)	87,52 (64,53 - 96,43)
Negative predictive value (95% CI) *	23,14 (17,24 - 30,33)	25,78 (21,34 - 30,78)	21,06 (19,19 - 23,05)

* assuming 80% prevalence

Renal abscesses were described in 3 patients with UTI (0.58%), accounting for 16.7% of infectious complications in UTI patients.
RUS performed during febrile UTI were compatible with vesicoureteral reflux (VUR) in 17.2% of the cases, leading to the execution of 80 voiding cystourethrogram (VCUG). VCUG confirmed VUR in 46.25% of the cases (VUR grade 1: 8.75%, VUR grade 2: 7.5%, VUR grade 3: 15%, VUR grade 4: 12.5%, VUR grade 5: 2.5%).
Conclusion: RUS is routinely performed during febrile UTI in pediatric patients. However, its contribution to UTI diagnosis was limited by poor performance metrics in our cohort. In terms of prognosis, RUS results evocative of congenital abnormalities of the kidney and urinary tract (CAKUT) compatible with VUR can offer a quicker access to VCUG.
Finally, RUS cost-benefit ratio remains debatable during non-complicated *E. coli* infections, or during a first episode of UTI in healthy children with no prior medical history evocative of CAKUT.

Miscellaneous (topic not included elsewhere)

P3-633 - Artificial intelligence to predict the individual risk of febrile urinary tract infection in children

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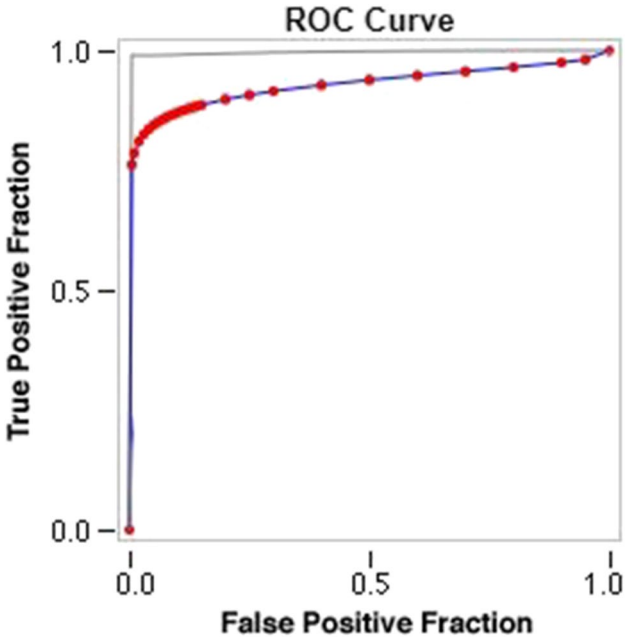
Background: Febrile urinary tract infections (UTI) are common in children. Timely diagnosis of pediatric febrile UTI is necessary to reduce infectious morbidity as well as antibiotic resistance and health costs.
However, confirmed UTI diagnosis requires validated urine cultures, which can take up to 3 days. Here we propose to use artificial intelligence to predict the risk of UTI in febrile children, using parameters available within the first hours of medical care.
Methods: We performed a retrospective study of medical and laboratory files of 61 pediatric patients with a suspected diagnosis of UTI, treated between 2014 and 2020 at the National Pediatric Reference Hospital of Luxembourg. Based on the results of urine cultures, patients were allocated to the UTI or control group. All patients were then randomly split into training and testing batches, used by a Random Forest algorithm to predict the individual risk of UTI, using clinical (age, sex), blood (CRP, white blood cell and neutrophil counts) and urine (red and white blood cell counts) parameters.
Results: Patients' demographic and clinical characteristics were comparable between groups. In particular, sex ratios were not significantly different between UTI and control patients.
Random Forest algorithm mean performance metrics were: accuracy 76.67% [63.96-86.62%], sensitivity 83.33% [68.64-93.03%], specificity 61.11% [35.75-82.70%]. Given a prevalence of UTI of 70%, positive predictive value was 83.33% [73.39-90.06%], negative predictive value 61.11% [42.11-77.24%]; mean AUC-ROC was 0.90 as shown in Figure 1.



Conclusion: Timely diagnosis of pediatric febrile UTI is necessary to minimize infectious morbidity, antibiotic resistance and health costs; however, it requires validated urine cultures, which can take several days. Here we showed that artificial intelligence can potentially predict

the individual risk of UTI in pediatric patients within the first hours of medical care, helping pediatricians in daily clinical decision making.

Miscellaneous (topic not included elsewhere)

P3-634 - Successful method to improve the consultation rate for the diagnostic work-up after the school urinalysis in Hachioji city.

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Introduction: The school urinalysis has been nationwide operation since 1973 in Japan, and its enforcement has been generalized. As the incidence of end stage renal disease caused by chronic glomerular disease had been remarkably decreased after the initiation of school urinalysis, the efficacy to improve the prognosis of chronic kidney disease has been widely recognized. The appropriate method of screening has been debated, and the Japan Society of Pediatric Nephrology had published its first manual for the school urinalysis. In this setting, importance of performing diagnostic work-up (DWU) after two step of urine dipstick screening is indicated. The site of DWU can be selected by municipal either mass operation by municipal (A-method) or the consultation to the medical institution (B-method). As the medical consultation in B-method is depending on child or guardian, the risk of decreasing rate for consultation is indicated and it was also the issue in Hachioji city under B-method operation.
Method: "Regional committee on school urinalysis (RCSU) of Hachioji city" is established for school urinalysis in 2014 and was co-operated by educational board of Hachioji city and pediatric department of regional medical association. Enlightenment of school urinalysis by educational board was re-confirmed. Modification in confirmation for DWU was also confirmed. We had instructed the guardians of the children to state and submit the "contact form (CF)" based on the informed consent by the physician instead of submitting "management guidance sheet (MGS)" noted by the physician.
Result: The submission rate of CF in 2014 was 37.8%, and progressive improvement was noted (2015:53.5%, 2017:56.7%, 2019:80.6%, and 2021:80.2%) after the establishment of LMSU. However, the stagnation of submission rate for MGS was still noted (2021:28%).
Conclusion: Successful improvement in consultation rate for DWU in B-method is confirmed after the establishment of RCSU.

Miscellaneous (topic not included elsewhere)

P3-636 - Assessment of Glomerulotubular Function of Children with Transfusion-Dependent Thalassemia

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Background: Thalassemia is the most common hemoglobinopathy found in South East Asia, particularly Indonesia. Dr. Cipto Mangunkusumo General Hospital, Indonesia's National Thalassemia Centre, treats 600-700 patients monthly. Chronic anemia, iron overload and iron chelating agents are factors that may cause kidney dysfunction in children with thalassemia. Urine neutrophil gelatinase-associated lipocalin (uNGAL) urine albumin creatinine ratio (uACr) are markers of glomerular and tubular damage in early chronic kidney disease.
Objective: To analyse glomerulotubular function in children with transfusion-dependent thalassemia.
Method: This prospective cohort study recruited children ≤18 years old with Transfusion Dependent Thalassemia (TDT) from the Thalassemia Transfusion Outpatient Clinic, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia between February – June 2021. History of disease and anthropometry measurements were obtained during enrolment (T0). Blood and urine samples were taken at enrolment (T0), 1 month (T1), 2 month (T2) and 3 month (T3) follow up. Data analysed were iron chelating agent, ferritin, serum creatinine, urine albumin creatinine ratio (uACr), and uNGAL levels. Abnormal uACR was defined as uACR >30 µg/mgCr.
Results: Forty TDT children were enrolled in this study. Median age was 14 (8-18) years, median blood transfusions per year was 19 (10-54) sessions. We observed lower proportion of patients with albuminuria and high proportion of patients with hyperfiltration across all timepoints (Table 1). We found a positive correlation between ferritin and uNGAL at T0 (r=0.301; p=0.067). Only one patient exhibited abnormal uNGAL (>150 ng/mL). There was no significant difference of uNGAL levels and albuminuria between patients receiving iron chelating agent deferasirox (DFX) and deferipone (DFP).
Conclusion: Assessment of glomerulotubular function showed hyperfiltration, albuminuria and normal uNGAL levels in most of children with TDT. uNGAL showed weak positive correlation to ferritin. Glomerulotubular function was similar in children receiving DFX and DFP.
Keywords: albuminuria, urinary NGAL, transfusion-dependent thalassemia, hyperfiltration

Miscellaneous (topic not included elsewhere)

P3-637 - Membership assessment of Twitter-based IPNA Journal Club (#IPNAJC) as a medical education tool-A pilot study

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Background: Free Open Access Medical Education (FOAMed) is successfully utilized by medical professionals worldwide to improve educational equity and networking opportunities. In alignment with the International Pediatric Nephrology Association's (IPNA) core vision, the social media sub-committee initiated a free, quarterly Twitter-based journal club (#IPNAJC) in July 2021.
Aim: To assess IPNA members' experience with IPNA-JC as a FOAMed tool.
Methods: An online, anonymous Survey Monkey-based 11-question survey was distributed to IPNA members by email between Nov–Dec 2021. Questions were designed as multiple-choice answers on a 1–5 Likert scale or narrative responses.
Results: Of 1900 members, 67 completed the survey (3.5% response rate), and most were from Asia (33%) (Figure 1A). Respondents were largely physicians (72%) and medical trainees (13%). Participants learned about #IPNAJC via email (69%), Twitter (16%), Colleagues (14%), and Facebook (1%). Approximately 42% participated live; the remaining participants interacted with the materials (summary, visual abstracts (VA), or curated chats) asynchronously. The majority (79%) reported that the timing was appropriate. The median (IQR) overall quality was 4 (3–5), quality of summaries was 4 (4–5), VA usefulness was 5 (5), and ease of participation in the discussion was 5 (3–5) (Figure 1B). Analysis of Twitter chat revealed that 65 people participated in the live #IPNAJC, generating 1331 tweets and 1.732 million impressions (mean) (Figure 1C).
Conclusion: The majority of respondents perceived that the #IPNAJC and FOAMed resources were of good quality. Poor response rate could be due to decreased awareness of #IPNAJC or unfamiliarity with Twitter. We intend to explore more widely used platforms for greater acceptability and reach. This survey study reinforces that FOAMed resources have a broad geographical reach, are accessed by users at all career stages, and can be utilized during and after a social media event.

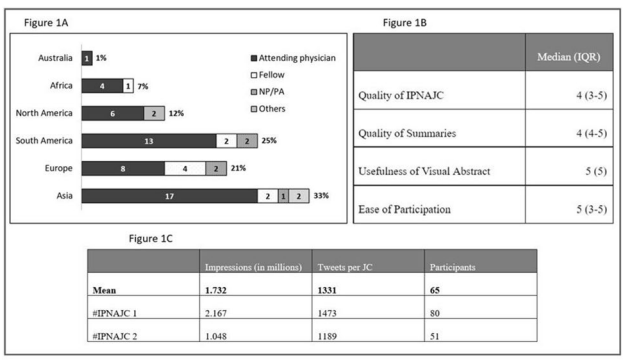

Figure 1: Demographics of survey participants (A), median quality scores for #IPNAJC and FOAMed materials (B) and Twitter metrics (C).

Miscellaneous (topic not included elsewhere)

P3-639 - Prevalence, correlates, and outcomes of glomerular hyperfiltration in children with cancer

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Background: Glomerular hyperfiltration has been reported in children with cancer but is poorly understood. Hyperfiltration has also been associated with acyclovir-induced AKI, though its relationship to complications during treatment for cancer has not been assessed.
Methods: This was a retrospective review, conducted across two tertiary paediatric hospitals, of two cohorts of children with cancer. One cohort consisted of patients undergoing allogeneic haematopoietic stem cell transplant (HSCT) for haematological malignancy at both sites, and the second consisted of children diagnosed with a solid organ malignancy at one site. All children had measured DTPA-GFR prior to treatment and estimated GFR (eGFR) was determined by modified Schwartz formula at 12 months after HSCT. Glomerular hyperfiltration was defined as GFR ≥160mL/min/1.73m2. We assessed for prevalence of hyperfiltration and associations between baseline characteristics and post-HSCT outcomes.
Results: There were 202 children in the HSCT cohort, and 91 in the solid organ malignancy cohort. Hyperfiltration was present in 17% of all children with cancer. Patients with hyperfiltration were younger (5.1 vs. 9.9 years; p=0.0055) and children with AML were more likely to hyperfilter than those with ALL (27% vs. 10%; p=0.02). Children with hyperfiltration had a higher weight increase in the first 30 days post-HSCT (7% vs. 4.7%; p=0.04). The majority (88%) of those hyperfiltering pre-HSCT returned to a normal eGFR at 1-year post transplant. At 1-year post-HSCT, 10.9% of children with normal kidney function developed hyperfiltration by eGFR. Acute GVHD was significantly associated with development of hyperfiltration at 1 year on multivariable analysis (OR 8.94, 95%CI 1.06-75.4; p=0.011).
Conclusion: Glomerular hyperfiltration occurs commonly in children with cancer, particularly younger patients and those with AML. Children with hyperfiltration may be at increased risk for fluid accumulation during HSCT. Hyperfiltration tends to resolve after HSCT, however acute GVHD is a risk factor for future development of hyperfiltration.

Miscellaneous (topic not included elsewhere)

P3-640 - Health Related Quality Of Life Amongst Children With Chronic Kidney Disease In Malaysia: Performance Of The Peds-Ql 3.0 ESRD Module Bahasa Melayu Version

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Holistic healthcare provision should include incorporation of patient-reported measures of health-related quality of life (HRQoL). The PedsQL 3.0 End Stage Renal Disease (ESRD) Module has been a well accepted instrument but this is not available in the local language. We aimed to assess the performance of the Bahasa Melayu version and determine HRQoL scores among children with CKD in Malaysia. METHODS: The source questionnaire in English was translated into Bahasa Melayu. Linguistic validation processes by the MAPI Research Institute were followed. The Bahasa Melayu PedsQL 4.0 Generic Core Scales was used as a comparator and sociodemographic data was collected. Statistical analyses performed using SPSS version 27.0. RESULTS: Sixty-nine children aged 8 to 18 with CKD 4 and 5,with or without dialysis and their caregivers were recruited. Mean age was 12.6 ± 2.77. Evaluation of the PedsQL 3.0 ESRD Module Bahasa Melayu version demonstrated good internal consistency (Cronbach alpha 0.82). There was good agreement between child self-report and parent-proxy report in all domains; average intraclass correlation coefficients (ICC) was 0.78, 95% CI (0.71,0.84). Scores obtained from Generic 4.0 scales correlated significantly with the disease specific ESRD 3.0 scale, Spearman's rho =0.32, p=0.007. Children with CKD 4 and 5 predialysis reported a relatively higher score: 72.79 (52.94-79.60) compared to their peers on dialysis; peritoneal dialysis group 58.82 (49.08-69.85) and hemodialysis group 59.56 (57.35-72.24). However, the Kruskal-Wallis H test indicated that this is not significantly different, $\chi 2(2) = 2.88$, $p = 0.236$. HRQoL scores were not affected by the carer's age, education level, marital status as well as duration of disease in this study.CONCLUSION: The PedsQL 3.0 ESRD Module Bahasa Melayu version is a reliable and feasible tool for cross-cultural adaptation. A longer prospective study may help illustrate the quality of life of these children better.

Miscellaneous (topic not included elsewhere)

P3-641 - How well is our adolescent population living with kidney disease: A nationwide multicentric prospective assessment of Quality of life in adolescents with CKD IV-V from India

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Introduction: Children with CKD IV-V with or without RRT,require frequent sampling for monitoring, invasive procedures and hospitalizations and have various complications related to their disease as well as therapy. No multicentric prospective studies have evaluated the QoL of children with CKD IV-V in developing countries. Acknowledging this theme for World Kidney Day 2021 was declared to be Living Well with Kidney Disease.Therefore we designed this study with aim of assessing self -reported Quality of life in adolescents with CKD IV-V using "Pediatric Quality of life (QoL) survey".
Objectives:
1. To determine important correlates of Quality of life in adoloscents with CKD IV-V
2. To compare the Qol between patients on dialysis vs those not initiated on dialysis and in children on maintenance Hemodialysis or Peritoneal dialysis with kidney transplant recipients.
Methodology: QoL to be assessed in adolescents (10-19 years of age) with CKD IV-V using "Pediatric Quality of life (QoL) survey" in a multicentric prospective study across major tertiary care institutes with Pediatric Nephrology units.
All adolescents with CKD IV-V based on eGFR estimated by modified Schwartz method are being included.Children with major co morbidities in other systems not directly related or consequence of kidney disease to be excluded
For all adolescents included in study personal particulars including details of family composition and socioeconomic condition of the family will be recorded as per proforma. They will be asked to fill the "Pediatric Quality of life (QoL) survey" in Hindi or English when they come to the hospital for scheduled review after written informed consent.Responses will be recorded and analyzed using Stata software.
Results: Adolescents with CKDIV-V are being enrolled across India.
Ack:This study was chosen as best project for WKD 2021 and we thank all the participating centres and our patients who consented to be part of this study

Miscellaneous (topic not included elsewhere)

P3-642 - Stepwise Approach to Loop Diuretic-Induced Secondary Hyperparathyroidism in Children

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Objectives: Describe the clinical features, laboratory findings and management of Loop Diuretic-induced Secondary Hyperparathyroidism (LD-SHPT) in children.
Methods: A single institution case series of LD-SHPT between 2015-2022.
Results: 6 infants (67% male), median age 4.5 months developed LD-SHPT from prolonged loop diuretic exposure (median 3.8 months). They presented with pathologic fractures (67%), incidental demineralization on radiographs (33%) and/or medullary nephrocalcinosis (33%). At presentation, median intact PTH was 266 pg/mL (range: 114-575) and alkaline phosphatase was 424 unit/L (range: 220-1200). Metabolic evaluation revealed appropriate serum 25-OH vitamin level, hypocalcemia in two infants (mean iCa 0.99 mmol/L), hypophosphatemia in one (2.6 mg/dL), and median urine calcium-to-creatinine ratio of 0.3 mg/mg (range 0.1-1.16). As first step to correct LD-SHPT, infants received supplementation with calcium, calcitriol, and maintenance ergocalciferol for a median of 71 days (range: 18-400). Concomitantly the infants were either started or dose escalated if on thiazide drugs. Three infants were successfully able to be weaned from loop diuretics with normalization of PTH, bone and mineral parameters. In the remaining three children the next step was to add cinacalet (0.25-0.4 mg/kg/day). Cinacalcet rapidly normalized PTH (median time 7 days; range: 3-8 days). The duration of cinacalcet therapy ranged from 2 weeks to 13 months. No patient developed significant hypocalcemia during

treatment. At last follow-up the median PTH was 59.4 pg/mL (range: 33.3–78.3 pg/mL), ALP was 190 unit/L (range: 136-358 unit/L), with normal mineral parameters and improved bone mineralization on radiographs.
Conclusion: We present a case series of children with LD-SHPT which is an underrecognized complication of long-term loop diuretic therapy. All efforts should be made to discontinue loop diuretics and convert to a thiazide diuretic, and initiate calcium and calcitriol supplementation. If still ineffective then cinacalcet should be considered. With this stepwise approach one can safely normalize the bone and mineral abnormalities associated with LD-SHPT.

Miscellaneous (topic not included elsewhere)

P3-643 - COVİD-19 vaccine-related side effects among adolescents with chronic kidney conditions: A single-center experience

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Objective: Considering the uncontrolled pandemic there is an urgent need for studies on the safety profile of the coronavirus disease-2019 (COVID-19) vaccination in children with chronic kidney conditions. Currently in Turkey COVID-19 vaccines are in use for the adolescent population. We aimed to investigate the side-effect and safety profile of COVİD-19 vaccines available for adolescents with chronic kidney disease (CKD) at our center.
Methods: Study population included patients with CKD stage 2–5, glomerular disease treated with immunosuppression, patients on dialysis and kidney transplant recipients followed-up during the pandemic. A questionnaire including demographic and medical information, history of COVID-19 infection, vaccination status, and vaccine-related side effects was administered to the patients.
Results: 98 patients (55 girls, 43 boys) were vaccinated by CoronaVac-inactived SARS-CoV-2 (n=16) or BNT162b2 messenger RNA (mRNA) COVİD-19 (n= 82) vaccine. The mean age was 16.90 ± 2,36 years and median follow-up 4,9 (0,5-11,03) months. There were 36 stage 2-5 CKD, 8 dialysis and 24 transplant patients in the cohort. The most common side effects were local pain (46,9 %), fatigue (17,3 %) and fever (11,2 %). No serious side effects were observed. Median duration of the symptoms was 2 (1-30) days. The longest symptom took 30 days; as dizziness in one patient with BNT162b2 mRNA vaccine. No renal disease flare was observed post-vaccination and 11 (11,2 %) patients experienced mild COVID-19 infection (according to NIH criteria). Although side effects with mRNA seemed more frequent than the inactivated vaccine, it was statistically insignificant (p=0,10). No significant relationship was found between frequency of side effects and age, glomerular filtration rate, immunosuppressive treatments, CKD stage and the underlying disease.
Conclusion: Although studies with longer follow-up are needed to evaluate the efficacy and side effects of COVID-19 vaccines, our early experience showed that vaccination is safe in the young population with CKD.

Miscellaneous (topic not included elsewhere)

P3-645 - Microdialysis in pediatric translational drug research: studying the tissue penetration of drugs in a juvenile pig model

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Background: Juvenile pig models have proven to provide an accurate and reliable prediction of pediatric pharmacokinetic behavior in plasma. However, the drug concentration in plasma often is a poor predictor for tissue disposition. Microdialysis is currently the gold standard for studying drug concentrations in tissues. In microdialysis, a small probe, consisting of a semipermeable hollow fiber membrane, is implanted into the tissue of interest. Mainly because of the semi-invasive character of microdialysis, tissue distribution of drugs remains largely understudied in children. The aim of this pilot study was to investigate the feasibility of multiple-day microdialysis in awake and free-moving juvenile piglets.
Methods: Twenty-two piglets of four weeks old were individually housed in pens. During short sedation, a microdialysis catheter was implanted in the paraspinal musculature under ultrasound guidance. Over the course of four days, intravenous antibiotics were administered and blood and microdialysis samples were taken while the piglets were awake and free moving in their pen.
Results: In seventeen of the twenty-two piglets, the microdialysis catheter remained functional until the end of the fourth sampling day. No adverse events (bleeding, infection, pain, or other discomforts) were observed during the placement of the microdialysis catheter and the whole study period. Antibiotic tissue concentration-time curves could be generated by means of calibration with an internal standard.
Conclusion: This study shows that it is feasible to use microdialysis to study tissue drug disposition in free moving piglets over multiple days, adding to the potential of this technique and the juvenile pig model in pediatric translational drug research.

Miscellaneous (topic not included elsewhere)

P3-646 - Health-related quality of life among siblings of kidney transplant recipients

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Studies are increasingly recognizing health-related quality of life (HRQOL) as a key pediatric outcome in both clinical and research settings and an essential health outcome measure to assess the effectiveness of medical treatment. However, it has not yet been studied among the healthy siblings of kidney transplant recipients.
The aim of this study, therefore, is to examine HRQOL among this population. We asked the following three groups to complete a validated

measure of HRQOL among children (KIDSCREEN-52): siblings of children who had received kidney transplants (n = 50), kidney transplant recipients (n = 43), and a healthy control group (n = 84).
We found that siblings of kidney transplant patients exhibited lower scores for financial resources and autonomy than kidney transplant recipients. They also served lower on physical well-being, financial resources, autonomy, and parent relations/home life than the control group. However, they scored higher on social acceptance than kidney transplant recipients. Our study underscores the importance of assessing HRQOL in families including a child diagnosed with a chronic illness.
Siblings require social and psychological support to promote coping and adaptation.
Keywords: chronic disease, health-related quality of life, kidney transplant recipients, siblings

Miscellaneous (topic not included elsewhere)

P3-648 - Specialized Summer 'Kidney Kamp' for Pediatric Nephrology Patients in Alberta, Canada

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Starting in 1995 with 6 children, 'Kidney Kamp' is an annual event at Camp Horizon in Southern Alberta. It is an opportunity for children between 8 and 18 years of age with chronic kidney disease (CKD) including those receiving kidney replacement therapies, kidney transplant, as well as other kidney diseases including cystinosis and nephrotic syndrome to participate in a weeklong overnight camp. Peritoneal dialysis takes place onsite while children requiring hemodialysis are transported 40 minutes to the Alberta Children's Hospital in Calgary for their hemodialysis procedure. The camp is supported by counsellors and specialized medical staff including nephrology nurses who attend camp the entire week and a nephrology dietitian who provides recommendations on camp meals and snacks.
With the popularity of Kidney Kamp, in 2003 it expanded to include children from across the entire province. Participants increased to between 35 and 40 campers per year, and nursing support was augmented to include staff from each of the two pediatric nephrology programs in the province, therefore increasing familiarity of camp staff with the campers. A pharmacist was also added to the team of specialized medical staff to help 'check in' medications and ensure organization for safe medication administration.
Through the week, camp participants were very busy with typical outdoor activities such as water sports, hiking, and climbing. There was also time for campfires, arts and crafts and the always very popular dance to celebrate the last night of camp.
Socialization and quality of life is important to children with chronic disease. Children with CKD thrive when around each other in this environment. This enables the campers to forge relationships that help them cope with living with kidney disease. Many who have attended Kidney Kamp have returned to participate in their Leadership Program to train and become counsellors for future camps.

Miscellaneous (topic not included elsewhere)

P3-649 - A single-center retrospective study of nephrocalcinosis in preschool-age children.

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Clinical presentation and etiologies of nephrocalcinosis (NC) are highly variable and there are controversies regarding whether NC leads to chronic kidney disease (CKD) or not. We aimed to evaluate the clinical outcome of preschool-age children with NC and compare the differences according to etiologies. We retrospectively reviewed the medical records of children with NC at Seoul National University Children's Hospital from 2004 to 2020. The inclusion criteria were as follows: 1) patients with NC aged 2 to 5 years; 2) patients who were followed up for 1 year or longer. We classified NC into three categories. A total of 86 children (boy:girl, 53:33) were diagnosed with NC at the median age of 0.75 (Interquartile ranges (IQR) 0.42-1.91) years. The etiology of NC included prematurity (32.6%), tubular disorders (24.4%), and others (43.0%). Seventy (81.4%) children were asymptomatic and had been diagnosed accidentally through the kidney ultrasonography. In 17 children (19.8%), the causative diseases were diagnosed because of NC, which included tubular disorders and primary hyperoxaluria. At a median follow-up of 4.2 (IQR 1.9-8.6) years, median urine calcium/creatinine ratio had significantly declined from 0.50 (0.24-1.06) mg/mg to 0.19 (0.08-0.35) mg/mg ($P<0.001$). CKD stage 2 (estimated glomerular filtration rate, eGFR <90 mL/min/1.73m^2) and growth impairment (height Z score < -1.88) were found in 43 (50.6%) and 28 (32.9%) patients, respectively, at the last follow-up. However, there were no statistical differences in the eGFR and height Z score between the diagnosis and the last follow-up point. While the proportion of CKD stage 2 significantly increased from 14.3% at the diagnosis to 59.3% at the last follow-up in the prematurity group ($P = 0.002$), there were no differences in the other groups. Early recognition and monitoring long-term kidney function of NC is clinically meaningful and may lead to further diagnosis.

Miscellaneous (topic not included elsewhere)

P3-650 - Single-cell transcriptomics reveal differential activation of Hippo signalling pathway in kidney cells

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Background: The Hippo signalling pathway is important in cell survival and polarity. "Inactivation" of this pathway leads to nuclear accumulation of Yes-Associated Protein (YAP)/transcriptional coactivator with PDZ-binding motif (TAZ), where they bind to TEA domain transcription factor (TEAD) 1-4 to form an activation complex. The latter then induces the Hippo target genes. Hippo pathway aberrations have been implicated in kidney diseases, though precise mechanisms are unknown. We aimed to analyse single-cell transcriptomics data to compare the activation status of the Hippo pathway in different kidney cells.
Methods: We analysed publicly available single-cell RNA-sequencing transcriptomics databases in human kidney tissues (GSE134355). Using evolutionary conserved YAP target genes, we performed Gene Set Enrich Analysis (GSEA) to compare the Hippo pathway activation

status in different cell clusters. We confirmed these findings using immunofluorescence (IMF) and immunohistochemistry (IHC) in normal human and rat kidney tissues to study the cellular distributions of YAP protein.

Results: Unsupervised transcriptomics database analysis defined 31 cell clusters with distinct gene expression patterns. Using cell markers, these clusters were classified into epithelial, endothelial, smooth muscle and immune cells. GSEA revealed differential activations of Hippo signaling pathway among each cell cluster, with endothelial cells showing a relatively higher transcription of YAP target genes. Among epithelial cells, podocytes and intercalated cells of collecting ducts showed the highest and lowest activation of YAP target genes respectively. We confirmed these results using IMF and IHC which showed intense YAP nuclear deposition in glomerular endothelium. Among epithelial cells, strong nuclear YAP was noted in podocytes and parietal epithelial cells, compared to faint signals in the proximal tubular nuclei. Rat tissue immunostaining corroborated with the human tissues, suggesting the differential activation of Hippo signalling is evolutionarily conserved.

Conclusion: We revealed heterogeneous activation status of the Hippo Signaling pathway in different kidney cell clusters.